(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 25 January 2001 (25.01.2001)

PCT

(10) International Publication Number WO 01/05970 A2

(51) International Patent Classification7: C12N 15/12, C07K 14/47, G01N 33/53, C12Q 1/68, A61K 38/17, C07K 16/18, A01K 67/027

(21) International Application Number: PCT/US00/19698

19 July 2000 (19.07.2000) (22) International Filing Date:

English (25) Filing Language:

English (26) Publication Language:

(30) Priority Data:

19 July 1999 (19.07.1999) US 60/144,595 23 August 1999 (23.08.1999) US 60/150,460 60/159,849 15 October 1999 (15.10.1999) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

60/144,595 (CIP) US 19 July 1999 (19.07.1999) Filed on US 60/150,460 (CIP) 23 August 1999 (23.08.1999) Filed on 60/159,849 (CIP) US Filed on 15 October 1999 (15.10.1999)

(71) Applicant (for all designated States except US): INCYTE GENOMICS, INC. [US/US]; 3160 Porter Drive, Palo Alto, CA 94304 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): YUE, Henry [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). BANDMAN, Olga [US/US]; 366 Anna Avenue, Mountain View, CA 94043 (US). HILLMAN, Jennifer, L. [US/US]; 230 Monroe Drive #12, Montain View, CA 94040 (US). LAL, Preeti [IN/US]; 2382 Lass Drive, Santa Clara, CA 95054 (US). AU-YOUNG, Janice [US/US]; 233 Golden Eagle Lane, Brisbane, CA 94005 (US). REDDY, Roopa [IN/US]; 1233 W. McKinley Avenue, #3, Sunnyvale, CA 94086 (US). YANG, Junming [CN/US]; 7125 Bark Lane, San Jose, CA 95129 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US). LU, Dyung, Aina, M. [US/US]; 55 Park Belmont Place, San Jose, CA 95136 (US). AZIMZAI, Yalda [US/US]; 2045 Rock Springs Drive, Hayward, CA 94545 (US). PATTERSON, Chandra [US/US]; 490 Sherwood Way #1, Menlo Park, CA 94025 (US).

- (74) Agents: HAMLET-COX, Diana et al.; Incyte Genomics, Inc., 3160 Porter Drive, Palo Alto, CA 94304 (US).
- (81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

Without international search report and to be republished upon receipt of that report.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

01/05970 A2

(54) Title: GTP-BINDING ASSOCIATED PROTEINS

(57) Abstract: The invention provides human GTP-binding associated proteins (GBAP) and polynucleotides which identify and encode GBAP. The invention also provides expression vectors, host cells, antibodies, agonist, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of GBAP.

GTP-BINDING ASSOCIATED PROTEINS

TECHNICAL FIELD

This invention relates to nucleic acid and amino acid sequences of GTP-binding associated proteins and to the use of these sequences in the diagnosis, treatment, and prevention of immune system, reproductive, nervous system, and cell signaling disorders, and cell proliferative disorders including cancer.

BACKGROUND OF THE INVENTION

10

Guanine nucleotide binding proteins (GTP-binding proteins) are present in all eukaryotic cells and function in processes including metabolism, cellular growth, differentiation, signal transduction, cytoskeletal organization, and intracellular vesicle transport and secretion. In higher organisms they are involved in signaling that regulates such processes as the immune response (Aussel, C. et al. (1988) J. Immunol. 140:215-220), apoptosis, differentiation, and cell proliferation including oncogenesis (Dhanasekaran, N. et al. (1998) Oncogene 17:1383-1394).

The superfamily of GTP-binding proteins can be subdivided into groups such as translational factors, heterotrimeric GTP-binding proteins involved in transmembrane signaling processes (also called G-proteins), proto-oncogene Ras proteins, other low molecular weight GTP-binding proteins including the products of rab, rap, rho, rac, smg21, smg25, YPT, SEC4, and ARF genes, and tubulins (Kaziro, Y. et al. (1991) Annu. Rev. Biochem. 60:349-400).

GTP-binding proteins are involved in protein biosynthesis and include initiation factor 2 (IF-2), elongation factor 2 (EF-Tu), and elongation factor G (EF-G), observed in prokaryotes; and initiation factor 2 (eIF-2), elongation factor Iα (EF-Iα), elongation factor 2 (EF-2), and release factor 3 (eRF3) observed in eukaryotes (Kaziro, supra). IF-2 promotes the GTP-dependent binding of the tRNA to the small subunit of the ribosome, the step that initiates protein translation. Elongation factors promote the binding of tRNA and GTP and the displacement of GDP after hydrolysis as protein biosynthesis proceeds. eRF3 participates in the recognition of stop codons and the release of nascent proteins from ribosomes.

Heterotrimeric GTP-binding proteins are composed of 3 subunits (α, β and γ) which, in the resting state, associate as a trimer at the inner face of the plasma membrane. Heterotrimeric G-proteins may be classified based on the sequence similarity of α subunits into the Gs, Gi, Gq and G12 subgroups. In the resting state, the α subunit binds guanosine diphosphate (GDP), and stimulation of the G-protein by an activated receptor leads to exchange of GDP for guanosine triphosphate (GTP).

35 This exchange results in the separation of the α from the β and γ subunits, which remain tightly

associated as a dimer. Both the α subunit and β - γ dimer are then able to interact with effectors, either individually or in a cooperative manner. The intrinsic GTPase activity of the α subunit hydrolyzes the bound GTP to GDP. This returns the α subunit to its inactive conformation and allows it to reassociate with the β - γ complex, thus restoring the system to its resting state (Kaziro, supra). Some α 5 subunits show tissue-specific expression indicating a specialized signaling role (Dhanasekaran, supra).

The α -s class of G-protein subunits is sensitive to ADP-ribosylation by pertussis toxin which uncouples the receptor:G-protein interaction. This uncoupling blocks signal transduction to receptors that decrease cAMP levels. cAMP levels regulate ion channels and activate phospholipases. The inhibitory α -I class is also susceptible to modification by pertussis toxin, which prevents α -I from lowering cAMP levels. Two novel classes of α subunits refractory to pertussis toxin modification are α -q, which activates phospholipase C, and α -12, which has sequence homology with the Drosophila gene concertina and may contribute to the regulation of embryonic development (Simon, M.I. (1991) Science 252:802-808).

The mammalian G-protein β and γ subunits, each about 340 amino acids long, share more than 80% homology. The β subunit (also called β-transducin) contains seven repeating units, each about 43 amino acids long. This WD-repeat, or G-beta repeat motif, is found in a variety of proteins with regulatory function such as Scc13, a yeast WD repeat protein involved in vesicular traffic; coronin-2, a mammalian WD repeat protein involved in regulation of the actin cytoskeleton; and Bop1, a mammalian WD repeat protein involved in growth suppression (Garcia-Higuera, I. et al. (1998) J. 20 Biol. Chem. 273:9041-9049; Okumura, M. et al. (1998) DNA Cell Biol. 17:779-787; Pestov, D.G. et al. (1998) Oncogene 17:3187-3197). The activity of the β and γ subunits may be regulated by other proteins such as calmodulin, phosducin, or the neural protein GAP 43 (Clapham, D.E. and E.J. Neer (1993) Nature 365:403-406). The β subunit sequences are highly conserved among species, suggesting that they perform a fundamentally important role in the organization and function of G-protein linked systems (Van der Voorn, L. and H.L. Ploegh (1992) FEBS Lett. 307:131-134).

Mutations and variant expression of β-transducin proteins are linked with various disorders. Mutations in LIS1, a subunit of the human platelet activating factor acetylhydrolase, cause Miller-Dieker lissencephaly. RACK1 binds activated protein kinase C, and RbAp48 binds retinoblastoma protein. CstF is required for polyadenylation of mammalian pre-mRNA in vitro and associates with subunits of cleavage-stimulating factor. Defects in the regulation of β-catenin contribute to the neoplastic transformation of human cells. The WD40 repeats of the human F-box protein βTrCP mediate binding to β-catenin, thus regulating the targeted degradation of β-catenin by ubiquitin ligase (Neer, E.J. et al. (1994) Nature 371:297-300; Hart, M. et al. (1999) Curr. Biol. 9:207-210).

The γ subunit sequences are more variable than those of the β subunits. They are often post-translationally modified by isoprenylation and carboxyl-methylation of a cysteine residue four amino

acids from the C-terminus. These modifications appear to be necessary for the interaction of the β-γ dimer with the membrane and with other GTP-binding proteins. The β-γ dimer has been shown to modulate the activity of adenylyl cyclase isoforms, phospholipase C, and some ion channels. It is involved in receptor phosphorylation via specific kinases and has been implicated in the p21ras-dependent activation of the MAP kinase cascade and the recognition of specific receptors by GTP-binding proteins (Clapham and Neer, supra).

G-proteins interact with a variety of effectors including adenylyl cyclase (Clapham and Neer, supra). The signaling pathway mediated by cAMP is mitogenic in hormone-dependent endocrine tissues such as adrenal cortex, thyroid, ovary, pituitary, and testes. Cancers in these tissues have been related to a mutationally activated form of a Gα, known as the gsp (Gs protein) oncogene (Dhanasekaran, supra). Another effector is phosducin, a retinal phosphoprotein, which forms a specific complex with retinal G-protein β and γ subunits and modulates the ability of the β-γ dimer to interact with retinal α subunits (Clapham and Neer, supra). Additional G-protein effectors include RIN1 (Ras interaction/interference), which acts as an effector of H-Ras and interferes with the Ras signal transduction pathway; Rabin3, which associates with the Ras-like GTPase Rab3A; and Rhotekin, a protein that binds with, and inhibits, Rho GTPase activity (Han, L. and J. Colicelli (1995) Mol. Cell Biol. 15:1318-1323; Brondyk, W.H. et al. (1995) Mol. Cell Biol. 15:1137-1143; and Reid, T. et al. (1996) J. Biol. Chem. 27:13556-13560).

The low molecular weight GTP-binding proteins regulate cell growth, cell cycle control, protein secretion, and intracellular vesicle interaction. These GTP-binding proteins respond to extracellular signals from receptors and activating proteins by transducing mitogenic signals (Tavitian, A. (1995) C. R. Seances Soc. Biol. Fil. 189:7-12). Low molecular weight GTP-binding proteins consist of single polypeptides of 21-30kD which, like the α subunit of heterotrimeric GTP-binding proteins, are able to bind to and hydrolyze GTP, thus cycling from an inactive to an active state. The intrinsic rate of GTP hydrolysis of these GTP-binding proteins is typically very slow, but it can be stimulated by several orders of magnitude by GTPase-activating proteins (GAPs), such as β2-chimaerin (Geyer, M. and Wittinghofer, A. (1997) Curr. Opin. Struct. Biol. 7:786-792; Caloca, M. J. et al. (1997) J. Biol. Chem. 272:26488-26496).

Low molecular weight GTP-binding proteins play critical roles in cellular protein trafficking

events, such as the translocation of proteins and soluble complexes from the cytosol to the membrane
through an exchange of GDP for GTP (Ktistakis, N.T. (1998) BioEssays 20:495-504). In vesicle
transport, the interaction between vesicle- and target- specific identifiers (v-SNAREs and tSNAREs)
docks the vesicle to the acceptor membrane. The budding process is regulated by GTPases such as the
closely related ADP ribosylation factors (ARFs) and SAR proteins, while GTPases such as Rab allow

assembly of SNARE complexes and may play a role in removal of defective complexes (Rothman, J.E.

and F.T. Wicland (1996) Science 272:227-234). The rab proteins control the translocation of vesicles to and from membranes for protein localization, protein processing, and secretion. The rho GTP-binding proteins control signal transduction pathways that link growth factor receptors to actin polymerization which is necessary for normal cellular growth and division. The ran GTP-binding proteins are located in the nucleus of cells and have a key role in nuclear protein import, the control of DNA synthesis, and cell-cycle progression (Hall, A. (1990) Science 249:635-640; Scheffzek, K. et al. (1995) Nature 374:378-381).

The Ras proteins Ras1, Ras2 and G₂α stimulate adenylyl cyclase (Kaziro, <u>supra</u>) which affects a broad array of cellular processes including determination of whether cells continue to grow or become terminally differentiated. Stimulation of cell surface receptors activates Ras which, in turn, activates cytoplasmic kinases. These kinases translocate to the nucleus and activate key transcription factors that control gene expression and protein synthesis (Barbacid, M. (1987) Annu. Rev. Biochem. 56:779-827; Treisman, R. (1994) Curr. Opin. Genet. Dev. 4:96-101). Mutant Ras-family proteins which bind but cannot hydrolyze GTP are permanently activated and are thus rendered oncogenic (Drivas, G.T. et al. (1990) Mol. Cell. Biol. 10:1793-1798).

Ras-like proteins have also been implicated in tumor suppression. For example, NOEY2, a novel gene encoding a Ras-like protein, is expressed in normal ovarian and breast epithelial cells. However, NOEY2 expression is reduced or abrogated in ovarian and breast carcinomas, suggesting a role for the NOEY2 gene product in tumor suppression (Yu, Y, et al. (1999) Proc. Natl. Acad. Sci. 20 USA 96:214-219).

Irregularities in GTP-binding protein signaling cascades may result in abnormal activation of leukocytes and lymphocytes, leading to the tissue damage and destruction seen in many inflammatory and autoimmune diseases such as rheumatoid arthritis, biliary cirrhosis, hemolytic anemia, lupus erythematosus, and thyroiditis. Abnormal cell proliferation, including cyclic AMP-mediated stimulation of brain, thyroid, adrenal, and gonadal tissue proliferation is regulated by G proteins. Mutations in G_α subunits have been found in growth-hormone-secreting pituitary somatotroph tumors, hyperfunctioning thyroid adenomas, and ovarian and adrenal neoplasms (Meij, J.T.A. (1996) Mol. Cell. Biochem. 157:31-38; Aussel, supra).

The discovery of new GTP-binding associated proteins and the polynucleotides encoding them satisfies a need in the art by providing new compositions which are useful in the diagnosis, prevention, and treatment of immune system, reproductive, nervous system, and cell signaling disorders, and cell proliferative disorders including cancer.

SUMMARY OF THE INVENTION

The invention features purified polypeptides, GTP-binding associated proteins, referred to

35

collectively as "GBAP" and individually as "GBAP-1," "GBAP-2," "GBAP-3," "GBAP-4," "GBAP-5," "GBAP-6," "GBAP-7," "GBAP-8," "GBAP-9," "GBAP-10," "GBAP-11," "GBAP-12," "GBAP-13," "GBAP-14," "GBAP-15," "GBAP-16," "GBAP-17," "GBAP-18," "GBAP-19," "GBAP-20," "GBAP-21," "GBAP-22," "GBAP-23," "GBAP-24," "GBAP-25," "GBAP-26," "GBAP-27," 5 "GBAP-28," "GBAP-29," "GBAP-30," "GBAP-31," "GBAP-32," "GBAP-33," "GBAP-34," "GBAP-35," "GBAP-36," "GBAP-37," "GBAP-38," "GBAP-39," "GBAP-40," "GBAP-41," "GBAP-42," "GBAP-43," "GBAP-44," "GBAP-45," "GBAP-46," "GBAP-47," "GBAP-48," "GBAP-49," "GBAP-50," "GBAP-51," "GBAP-52," "GBAP-53," "GBAP-54," "GBAP-55," "GBAP-56," "GBAP-57," "GBAP-58," "GBAP-59," "GBAP-60," "GBAP-61," "GBAP-62," 10 "GBAP-63," "GBAP-64," "GBAP-65," and "GBAP-66." In one aspect, the invention provides an isolated polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino acid sequence 15 selected from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66. In one alternative, the invention provides an isolated polypeptide comprising the amino acid sequence of SEO ID NO:1-66.

The invention further provides an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66. In one alternative, the polynucleotide encodes a polypeptide selected from the group consisting of SEQ ID NO:1-66. In another alternative, the polynucleotide is selected from the group consisting of SEQ ID NO:1-32.

Additionally, the invention provides a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66. In one alternative, the invention provides a cell transformed with the recombinant polynucleotide. In another alternative, the invention provides a transgenic organism

comprising the recombinant polynucleotide.

The invention also provides a method for producing a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66. The method comprises a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide encoding the polypeptide, and b) recovering the polypeptide so expressed.

Additionally, the invention provides an isolated antibody which specifically binds to a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66.

The invention further provides an isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, b) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, c) a polynucleotide sequence complementary to a), d) a polynucleotide sequence complementary to b), and e) an RNA equivalent of a)-d). In one alternative, the polynucleotide comprises at least 60 contiguous nucleotides.

Additionally, the invention provides a method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, b) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, c) a polynucleotide sequence complementary to a), d) a polynucleotide sequence complementary to b), and e) an RNA equivalent of a)-d). The method comprises a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or

fragments thereof, and b) detecting the presence or absence of said hybridization complex, and optionally, if present, the amount thereof. In one alternative, the probe comprises at least 60 contiguous nucleotides.

The invention further provides a method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, b) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, c) a polynucleotide sequence complementary to a), d) a polynucleotide sequence complementary to b), and e) an RNA equivalent of a)-d). The method comprises a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

The invention further provides a composition comprising an effective amount of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, and a pharmaceutically acceptable excipient. In one embodiment, the 1 composition comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-66. The invention additionally provides a method of treating a disease or condition associated with decreased expression of functional GBAP, comprising administering to a patient in need of such treatment the composition.

The invention also provides a method for screening a compound for effectiveness as an agonist of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66. The method comprises a) exposing a sample comprising the polypeptide to a compound, and b) detecting agonist activity in the sample. In one alternative, the invention provides a composition comprising an agonist compound identified by the method and a pharmaceutically acceptable excipient. In another alternative, the invention provides a method of treating a disease or condition associated with decreased expression of

PCT/US00/19698 WO 01/05970

functional GBAP, comprising administering to a patient in need of such treatment the composition.

Additionally, the invention provides a method for screening a compound for effectiveness as an antagonist of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally 5 occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66. The method comprises a) exposing a sample comprising the polypeptide to a compound, and b) detecting 10 antagonist activity in the sample. In one alternative, the invention provides a composition comprising an antagonist compound identified by the method and a pharmaceutically acceptable excipient. In another alternative, the invention provides a method of treating a disease or condition associated with overexpression of functional GBAP, comprising administering to a patient in need of such treatment the composition.

The invention further provides a method of screening for a compound that specifically binds 15 to a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino acid sequence selected 20 from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66. The method comprises a) combining the polypeptide with at least one test compound under suitable conditions, and b) detecting binding of the polypeptide to the test compound, thereby identifying a compound that specifically binds to the polypeptide.

The invention further provides a method of screening for a compound that modulates the activity of a polypeptide comprising an amino acid sequence selected from the group consisting of a) an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1-66, c) a biologically active fragment of an amino 30 acid sequence selected from the group consisting of SEQ ID NO:1-66, and d) an immunogenic fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1-66. The method comprises a) combining the polypeptide with at least one test compound under conditions permissive for the activity of the polypeptide, b) assessing the activity of the polypeptide in the presence of the test compound, and c) comparing the activity of the polypeptide in the presence of the 35 test compound with the activity of the polypeptide in the absence of the test compound, wherein a

25

change in the activity of the polypeptide in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide.

The invention further provides a method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence selected from the group consisting of SEQ ID NO:67-132, the method comprising a) exposing a sample comprising the target polynucleotide to a compound, and b) detecting altered expression of the target polynucleotide.

The invention further provides a method for assessing toxicity of a test compound, said method comprising a) treating a biological sample containing nucleic acids with the test compound; 10 b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide comprising a polynucleotide sequence selected from the group consisting of i) a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, ii) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, iii) a 15 polynucleotide sequence complementary to i), iv) a polynucleotide sequence complementary to ii), and v) an RNA equivalent of i)-iv). Hybridization occurs under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, ii) a naturally occurring polynucleotide sequence having at least 20 70% sequence identity to a polynucleotide sequence selected from the group consisting of SEQ ID NO:67-132, iii) a polynucleotide sequence complementary to i), iv) a polynucleotide sequence complementary to ii), and v) an RNA equivalent of i)-iv). Alternatively, the target polynucleotide comprises a fragment of the above polynucleotide sequence; c) quantifying the amount of hybridization complex; and d) comparing the amount of hybridization complex in the treated 25 biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

BRIEF DESCRIPTION OF THE TABLES

Table 1 shows polypeptide and nucleotide sequence identification numbers (SEQ ID NOs), clone identification numbers (clone IDs), cDNA libraries, and cDNA fragments used to assemble full-length sequences encoding GBAP.

30

Table 2 shows features of each polypeptide sequence, including potential motifs, homologous sequences, and methods, algorithms, and searchable databases used for analysis of GBAP.

Table 3 shows selected fragments of each nucleic acid sequence; the tissue-specific expression

patterns of each nucleic acid sequence as determined by northern analysis; diseases, disorders, or conditions associated with these tissues; and the vector into which each cDNA was cloned.

Table 4 describes the tissues used to construct the cDNA libraries from which cDNA clones encoding GBAP were isolated.

Table 5 shows the tools, programs, and algorithms used to analyze the polynucleotides and polypeptides of the invention, along with applicable descriptions, references, and threshold parameters.

DESCRIPTION OF THE INVENTION

Before the present proteins, nucleotide sequences, and methods are described, it is understood that this invention is not limited to the particular machines, materials and methods described, as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural reference unless the context clearly dictates otherwise. Thus, for example, a reference to "a host cell" includes a plurality of such host cells, and a reference to "an antibody" is a reference to one or more antibodies and equivalents thereof known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings
as commonly understood by one of ordinary skill in the art to which this invention belongs. Although
any machines, materials, and methods similar or equivalent to those described herein can be used to
practice or test the present invention, the preferred machines, materials and methods are now described.
All publications mentioned herein are cited for the purpose of describing and disclosing the cell lines,
protocols, reagents and vectors which are reported in the publications and which might be used in
connection with the invention. Nothing herein is to be construed as an admission that the invention is
not entitled to antedate such disclosure by virtue of prior invention.

DEFINITIONS

"GBAP" refers to the amino acid sequences of substantially purified GBAP obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and human, and from any source, whether natural, synthetic, semi-synthetic, or recombinant.

The term "agonist" refers to a molecule which intensifies or mimics the biological activity of GBAP. Agonists may include proteins, nucleic acids, carbohydrates, small molecules, or any other compound or composition which modulates the activity of GBAP either by directly interacting with GBAP or by acting on components of the biological pathway in which GBAP participates.

An "allelic variant" is an alternative form of the gene encoding GBAP. Allelic variants may

result from at least one mutation in the nucleic acid sequence and may result in altered mRNAs or in polypeptides whose structure or function may or may not be altered. A gene may have none, one, or many allelic variants of its naturally occurring form. Common mutational changes which give rise to allelic variants are generally ascribed to natural deletions, additions, or substitutions of nucleotides.

5 Each of these types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

"Altered" nucleic acid sequences encoding GBAP include those sequences with deletions, insertions, or substitutions of different nucleotides, resulting in a polypeptide the same as GBAP or a polypeptide with at least one functional characteristic of GBAP. Included within this definition are 10 polymorphisms which may or may not be readily detectable using a particular oligonucleotide probe of the polynucleotide encoding GBAP, and improper or unexpected hybridization to allelic variants, with a locus other than the normal chromosomal locus for the polynucleotide sequence encoding GBAP. The encoded protein may also be "altered," and may contain deletions, insertions, or substitutions of amino acid residues which produce a silent change and result in a functionally equivalent GBAP. Deliberate 15 amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues, as long as the biological or immunological activity of GBAP is retained. For example, negatively charged amino acids may include aspartic acid and glutamic acid, and positively charged amino acids may include lysine and arginine. Amino acids with uncharged polar side chains having similar hydrophilicity values may 20 include: asparagine and glutamine; and serine and threonine. Amino acids with uncharged side chains having similar hydrophilicity values may include: leucine, isoleucine, and valine; glycine and alanine; and phenylalanine and tyrosine.

The terms "amino acid" and "amino acid sequence" refer to an oligopeptide, peptide, polypeptide, or protein sequence, or a fragment of any of these, and to naturally occurring or synthetic molecules. Where "amino acid sequence" is recited to refer to a sequence of a naturally occurring protein molecule, "amino acid sequence" and like terms are not meant to limit the amino acid sequence to the complete native amino acid sequence associated with the recited protein molecule.

"Amplification" relates to the production of additional copies of a nucleic acid sequence.

Amplification is generally carried out using polymerase chain reaction (PCR) technologies well known

30 in the art.

The term "antagonist" refers to a molecule which inhibits or attenuates the biological activity of GBAP. Antagonists may include proteins such as antibodies, nucleic acids, carbohydrates, small molecules, or any other compound or composition which modulates the activity of GBAP either by directly interacting with GBAP or by acting on components of the biological pathway in which GBAP participates.

The term "antibody" refers to intact immunoglobulin molecules as well as to fragments thereof, such as Fab, F(ab')₂, and Fv fragments, which are capable of binding an epitopic determinant.

Antibodies that bind GBAP polypeptides can be prepared using intact polypeptides or using fragments containing small peptides of interest as the immunizing antigen. The polypeptide or oligopeptide used to immunize an animal (e.g., a mouse, a rat, or a rabbit) can be derived from the translation of RNA, or synthesized chemically, and can be conjugated to a carrier protein if desired. Commonly used carriers that are chemically coupled to peptides include bovine serum albumin, thyroglobulin, and keyhole limpet hemocyanin (KLH). The coupled peptide is then used to immunize the animal.

The term "antigenic determinant" refers to that region of a molecule (i.e., an epitope) that

10 makes contact with a particular antibody. When a protein or a fragment of a protein is used to
immunize a host animal, numerous regions of the protein may induce the production of antibodies which
bind specifically to antigenic determinants (particular regions or three-dimensional structures on the
protein). An antigenic determinant may compete with the intact antigen (i.e., the immunogen used to
elicit the immune response) for binding to an antibody.

The term "antisense" refers to any composition capable of base-pairing with the "sense" (coding) strand of a specific nucleic acid sequence. Antisense compositions may include DNA; RNA; peptide nucleic acid (PNA); oligonucleotides having modified backbone linkages such as phosphorothioates, methylphosphonates, or benzylphosphonates; oligonucleotides having modified sugar groups such as 2'-methoxyethyl sugars or 2'-methoxyethoxy sugars; or oligonucleotides having modified bases such as 5-methyl cytosine, 2'-deoxyuracil, or 7-deaza-2'-deoxyguanosine. Antisense molecules may be produced by any method including chemical synthesis or transcription. Once introduced into a cell, the complementary antisense molecule base-pairs with a naturally occurring nucleic acid sequence produced by the cell to form duplexes which block either transcription or translation. The designation "negative" or "minus" can refer to the antisense strand, and the

The term "biologically active" refers to a protein having structural, regulatory, or biochemical functions of a naturally occurring molecule. Likewise, "immunologically active" or "immunogenic" refers to the capability of the natural, recombinant, or synthetic GBAP, or of any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

"Complementary" describes the relationship between two single-stranded nucleic acid sequences that anneal by base-pairing. For example, 5'-AGT-3' pairs with its complement, 3'-TCA-5'.

A "composition comprising a given polynucleotide sequence" and a "composition comprising a given amino acid sequence" refer broadly to any composition containing the given polynucleotide or

amino acid sequence. The composition may comprise a dry formulation or an aqueous solution.

Compositions comprising polynucleotide sequences encoding GBAP or fragments of GBAP may be employed as hybridization probes. The probes may be stored in freeze-dried form and may be associated with a stabilizing agent such as a carbohydrate. In hybridizations, the probe may be deployed in an aqueous solution containing salts (e.g., NaCl), detergents (e.g., sodium dodecyl sulfate; SDS), and other components (e.g., Denhardt's solution, dry milk, salmon sperm DNA, etc.).

"Consensus sequence" refers to a nucleic acid sequence which has been subjected to repeated DNA sequence analysis to resolve uncalled bases, extended using the XL-PCR kit (PE Biosystems, Foster City CA) in the 5' and/or the 3' direction, and resequenced, or which has been assembled from one or more overlapping cDNA, EST, or genomic DNA fragments using a computer program for fragment assembly, such as the GELVIEW fragment assembly system (GCG, Madison WI) or Phrap (University of Washington, Seattle WA). Some sequences have been both extended and assembled to produce the consensus sequence.

"Conservative amino acid substitutions" are those substitutions that are predicted to least

15 interfere with the properties of the original protein, i.e., the structure and especially the function of the protein is conserved and not significantly changed by such substitutions. The table below shows amino acids which may be substituted for an original amino acid in a protein and which are regarded as conservative amino acid substitutions.

	Original Residue	Conservative Substitution
20	Ala	Gly, Ser
	Arg	His, Lys
	Asn	Asp, Gln, His
	Asp	Asn, Glu
	Cys	Ala, Ser
25	Gln	Asn, Glu, His
	Glu	Asp, Gln, His
	Gly	Ala
	. His	Asn, Arg, Gln, Glu
	Ne	Leu, Val
30	Leu	Ile, Val
	Lys	Arg, Gln, Glu
	Met	Leu, Ile
	Phe	His, Met, Leu, Trp, Tyr
	Ser	Cys, Thr
35	Thr	Ser, Val
	Trp	Phe, Tyr
	Туг	His, Phe, Trp
	Val	Ile, Leu, Thr

Conservative amino acid substitutions generally maintain (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a beta sheet or alpha helical conformation, (b) the charge or hydrophobicity of the molecule at the site of the substitution, and/or (c) the bulk of the

side chain.

10

A "deletion" refers to a change in the amino acid or nucleotide sequence that results in the absence of one or more amino acid residues or nucleotides.

The term "derivative" refers to a chemically modified polynucleotide or polypeptide. Chemical modifications of a polynucleotide sequence can include, for example, replacement of hydrogen by an alkyl, acyl, hydroxyl, or amino group. A derivative polynucleotide encodes a polypeptide which retains at least one biological or immunological function of the natural molecule. A derivative polypeptide is one modified by glycosylation, pegylation, or any similar process that retains at least one biological or immunological function of the polypeptide from which it was derived.

A "detectable label" refers to a reporter molecule or enzyme that is capable of generating a measurable signal and is covalently or noncovalently joined to a polynucleotide or polypeptide.

A "fragment" is a unique portion of GBAP or the polynucleotide encoding GBAP which is identical in sequence to but shorter in length than the parent sequence. A fragment may comprise up to the entire length of the defined sequence, minus one nucleotide/amino acid residue. For example, a fragment may comprise from 5 to 1000 contiguous nucleotides or amino acid residues. A fragment used as a probe, primer, antigen, therapeutic molecule, or for other purposes, may be at least 5, 10, 15, 16, 20, 25, 30, 40, 50, 60, 75, 100, 150, 250 or at least 500 contiguous nucleotides or amino acid residues in length. Fragments may be preferentially selected from certain regions of a molecule. For example, a polypeptide fragment may comprise a certain length of contiguous amino acids selected from the first 250 or 500 amino acids (or first 25% or 50% of a polypeptide) as shown in a certain defined sequence. Clearly these lengths are exemplary, and any length that is supported by the specification, including the Sequence Listing, tables, and figures, may be encompassed by the present embodiments.

A fragment of SEQ ID NO:67-132 comprises a region of unique polynucleotide sequence that specifically identifies SEQ ID NO:67-132, for example, as distinct from any other sequence in the genome from which the fragment was obtained. A fragment of SEQ ID NO:67-132 is useful, for example, in hybridization and amplification technologies and in analogous methods that distinguish SEQ ID NO:67-132 from related polynucleotide sequences. The precise length of a fragment of SEQ ID NO:67-132 and the region of SEQ ID NO:67-132 to which the fragment corresponds are routinely determinable by one of ordinary skill in the art based on the intended purpose for the fragment.

A fragment of SEQ ID NO:1-66 is encoded by a fragment of SEQ ID NO:67-132. A fragment of SEQ ID NO:1-66 comprises a region of unique amino acid sequence that specifically identifies SEQ ID NO:1-66. For example, a fragment of SEQ ID NO:1-66 is useful as an immunogenic peptide for the development of antibodies that specifically recognize SEQ ID NO:1-66.

The precise length of a fragment of SEQ ID NO:1-66 and the region of SEQ ID NO:1-66 to which the

fragment corresponds are routinely determinable by one of ordinary skill in the art based on the intended purpose for the fragment.

A "full-length" polynucleotide sequence is one containing at least a translation initiation codon (e.g., methionine) followed by an open reading frame and a translation termination codon. A "full-slength" polynucleotide sequence encodes a "full-length" polypeptide sequence.

"Homology" refers to sequence similarity or, interchangeably, sequence identity, between two or more polynucleotide sequences or two or more polypeptide sequences.

The terms "percent identity" and "% identity," as applied to polynucleotide sequences, refer to the percentage of residue matches between at least two polynucleotide sequences aligned using a standardized algorithm. Such an algorithm may insert, in a standardized and reproducible way, gaps in the sequences being compared in order to optimize alignment between two sequences, and therefore achieve a more meaningful comparison of the two sequences.

Percent identity between polynucleotide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence 15 alignment program. This program is part of the LASERGENE software package, a suite of molecular biological analysis programs (DNASTAR, Madison WI). CLUSTAL V is described in Higgins, D.G. and P.M. Sharp (1989) CABIOS 5:151-153 and in Higgins, D.G. et al. (1992) CABIOS 8:189-191. For pairwise alignments of polynucleotide sequences, the default parameters are set as follows:

Ktuple=2, gap penalty=5, window=4, and "diagonals saved"=4. The "weighted" residue weight table is selected as the default. Percent identity is reported by CLUSTAL V as the "percent similarity" between aligned polynucleotide sequences.

Alternatively, a suite of commonly used and freely available sequence comparison algorithms is provided by the National Center for Biotechnology Information (NCBI) Basic Local Alignment Search Tool (BLAST) (Altschul, S.F. et al. (1990) J. Mol. Biol. 215:403-410), which is available from several sources, including the NCBI, Bethesda, MD, and on the Internet at http://www.ncbi.nlm.nih.gov/BLAST/. The BLAST software suite includes various sequence analysis programs including "blastn," that is used to align a known polynucleotide sequence with other polynucleotide sequences from a variety of databases. Also available is a tool called "BLAST 2 Sequences" that is used for direct pairwise comparison of two nucleotide sequences. "BLAST 2 Sequences" can be accessed and used interactively at http://www.ncbi.nlm.nih.gov/gorf/bl2.html. The "BLAST 2 Sequences" tool can be used for both blastn and blastp (discussed below). BLAST programs are commonly used with gap and other parameters set to default settings. For example, to compare two nucleotide sequences, one may use blastn with the "BLAST 2 Sequences" tool Version

Matrix: BLOSUM62

35

2.0.12 (April-21-2000) set at default parameters. Such default parameters may be, for example:

Reward for match: 1

Penalty for mismatch: -2

Open Gap: 5 and Extension Gap: 2 penalties

Gap x drop-off: 50

5 *Expect: 10*

Word Size: 11

Filter: on

Percent identity may be measured over the length of an entire defined sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined sequence, for instance, a fragment of at least 20, at least 30, at least 40, at least 50, at least 70, at least 100, or at least 200 contiguous nucleotides. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures, or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

Nucleic acid sequences that do not show a high degree of identity may nevertheless encode similar amino acid sequences due to the degeneracy of the genetic code. It is understood that changes in a nucleic acid sequence can be made using this degeneracy to produce multiple nucleic acid sequences that all encode substantially the same protein.

The phrases "percent identity" and "% identity," as applied to polypeptide sequences, refer to

20 the percentage of residue matches between at least two polypeptide sequences aligned using a

standardized algorithm. Methods of polypeptide sequence alignment are well-known. Some alignment

methods take into account conservative amino acid substitutions. Such conservative substitutions,

explained in more detail above, generally preserve the charge and hydrophobicity at the site of

substitution, thus preserving the structure (and therefore function) of the polypeptide.

Percent identity between polypeptide sequences may be determined using the default parameters of the CLUSTAL V algorithm as incorporated into the MEGALIGN version 3.12e sequence alignment program (described and referenced above). For pairwise alignments of polypeptide sequences using CLUSTAL V, the default parameters are set as follows: Ktuple=1, gap penalty=3, window=5, and "diagonals saved"=5. The PAM250 matrix is selected as the default residue weight table. As with polynucleotide alignments, the percent identity is reported by CLUSTAL V as the "percent similarity" between aligned polypeptide sequence pairs.

Alternatively the NCBI BLAST software suite may be used. For example, for a pairwise comparison of two polypeptide sequences, one may use the "BLAST 2 Sequences" tool Version 2.0.12 (Apr-21-2000) with blastp set at default parameters. Such default parameters may be, for example:

Matrix: BLOSUM62

35

Open Gap: 11 and Extension Gap: 1 penalties

Gap x drop-off: 50

Expect: 10
Word Size: 3

5 Filter: on

Percent identity may be measured over the length of an entire defined polypeptide sequence, for example, as defined by a particular SEQ ID number, or may be measured over a shorter length, for example, over the length of a fragment taken from a larger, defined polypeptide sequence, for instance, a fragment of at least 15, at least 20, at least 30, at least 40, at least 50, at least 70 or at least 150 contiguous residues. Such lengths are exemplary only, and it is understood that any fragment length supported by the sequences shown herein, in the tables, figures or Sequence Listing, may be used to describe a length over which percentage identity may be measured.

"Human artificial chromosomes" (HACs) are linear microchromosomes which may contain DNA sequences of about 6 kb to 10 Mb in size, and which contain all of the elements required for thromosome replication, segregation and maintenance.

The term "humanized antibody" refers to an antibody molecule in which the amino acid sequence in the non-antigen binding regions has been altered so that the antibody more closely resembles a human antibody, and still retains its original binding ability.

"Hybridization" refers to the process by which a polynucleotide strand anneals with a
20 complementary strand through base pairing under defined hybridization conditions. Specific hybridization is an indication that two nucleic acid sequences share a high degree of complementarity. Specific hybridization complexes form under permissive annealing conditions and remain hybridized after the "washing" step(s). The washing step(s) is particularly important in determining the stringency of the hybridization process, with more stringent conditions allowing less non-specific binding, i.e.,
25 binding between pairs of nucleic acid strands that are not perfectly matched. Permissive conditions for annealing of nucleic acid sequences are routinely determinable by one of ordinary skill in the art and may be consistent among hybridization experiments, whereas wash conditions may be varied among experiments to achieve the desired stringency, and therefore hybridization specificity. Permissive annealing conditions occur, for example, at 68°C in the presence of about 6 x SSC, about 1% (w/v)
30 SDS, and about 100 μg/ml sheared, denatured salmon sperm DNA.

Generally, stringency of hybridization is expressed, in part, with reference to the temperature under which the wash step is carried out. Such wash temperatures are typically selected to be about 5° C to 20° C lower than the thermal melting point ($T_{\rm m}$) for the specific sequence at a defined ionic strength and pH. The $T_{\rm m}$ is the temperature (under defined ionic strength and pH) at which 50% of the target sequence hybridizes to a perfectly matched probe. An equation for calculating $T_{\rm m}$ and conditions

PCT/US00/19698 WO 01/05970

for nucleic acid hybridization are well known and can be found in Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY; specifically see volume 2, chapter 9.

High stringency conditions for hybridization between polynucleotides of the present invention 5 include wash conditions of 68°C in the presence of about 0.2 x SSC and about 0.1% SDS, for 1 hour. Alternatively, temperatures of about 65°C, 60°C, 55°C, or 42°C may be used. SSC concentration may be varied from about 0.1 to 2 x SSC, with SDS being present at about 0.1%. Typically, blocking reagents are used to block non-specific hybridization. Such blocking reagents include, for instance, sheared and denatured salmon sperm DNA at about 100-200 µg/ml. Organic solvent, such as 10 formamide at a concentration of about 35-50% v/v, may also be used under particular circumstances, such as for RNA:DNA hybridizations. Useful variations on these wash conditions will be readily apparent to those of ordinary skill in the art. Hybridization, particularly under high stringency conditions, may be suggestive of evolutionary similarity between the nucleotides. Such similarity is strongly indicative of a similar role for the nucleotides and their encoded polypeptides.

The term "hybridization complex" refers to a complex formed between two nucleic acid sequences by virtue of the formation of hydrogen bonds between complementary bases. A hybridization complex may be formed in solution (e.g., Cot or Rot analysis) or formed between one nucleic acid sequence present in solution and another nucleic acid sequence immobilized on a solid support (e.g., paper, membranes, filters, chips, pins or glass slides, or any other appropriate substrate to which cells 20 or their nucleic acids have been fixed).

15

35

The words "insertion" and "addition" refer to changes in an amino acid or nucleotide sequence resulting in the addition of one or more amino acid residues or nucleotides, respectively.

"Immune response" can refer to conditions associated with inflammation, trauma, immune disorders, or infectious or genetic disease, etc. These conditions can be characterized by expression of 25 various factors, e.g., cytokines, chemokines, and other signaling molecules, which may affect cellular and systemic defense systems.

An "immunogenic fragment" is a polypeptide or oligopeptide fragment of GBAP which is capable of eliciting an immune response when introduced into a living organism, for example, a mammal. The term "immunogenic fragment" also includes any polypeptide or oligopeptide fragment of 30 GBAP which is useful in any of the antibody production methods disclosed herein or known in the art.

The term "microarray" refers to an arrangement of a plurality of polynucleotides, polypeptides, or other chemical compounds on a substrate.

The terms "element" and "array element" refer to a polynucleotide, polypeptide, or other chemical compound having a unique and defined position on a microarray.

The term "modulate" refers to a change in the activity of GBAP. For example, modulation

may cause an increase or a decrease in protein activity, binding characteristics, or any other biological, functional, or immunological properties of GBAP.

The phrases "nucleic acid" and "nucleic acid sequence" refer to a nucleotide, oligonucleotide, polynucleotide, or any fragment thereof. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA), or to any DNA-like or RNA-like material.

"Operably linked" refers to the situation in which a first nucleic acid sequence is placed in a functional relationship with a second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Operably linked DNA sequences may be in close proximity or contiguous and, where necessary to join two protein coding regions, in the same reading frame.

"Peptide nucleic acid" (PNA) refers to an antisense molecule or anti-gene agent which comprises an oligonucleotide of at least about 5 nucleotides in length linked to a peptide backbone of amino acid residues ending in lysine. The terminal lysine confers solubility to the composition. PNAs preferentially bind complementary single stranded DNA or RNA and stop transcript elongation, and may be pegylated to extend their lifespan in the cell.

"Post-translational modification" of an GBAP may involve lipidation, glycosylation, phosphorylation, acetylation, racemization, proteolytic cleavage, and other modifications known in the art. These processes may occur synthetically or biochemically. Biochemical modifications will vary by cell type depending on the enzymatic milieu of GBAP.

"Probe" refers to nucleic acid sequences encoding GBAP, their complements, or fragments thereof, which are used to detect identical, allelic or related nucleic acid sequences. Probes are isolated oligonucleotides or polynucleotides attached to a detectable label or reporter molecule. Typical labels include radioactive isotopes, ligands, chemiluminescent agents, and enzymes. "Primers" are short nucleic acids, usually DNA oligonucleotides, which may be annealed to a target polynucleotide by complementary base-pairing. The primer may then be extended along the target DNA strand by a DNA polymerase enzyme. Primer pairs can be used for amplification (and identification) of a nucleic acid sequence, e.g., by the polymerase chain reaction (PCR).

Probes and primers as used in the present invention typically comprise at least 15 contiguous nucleotides of a known sequence. In order to enhance specificity, longer probes and primers may also be employed, such as probes and primers that comprise at least 20, 25, 30, 40, 50, 60, 70, 80, 90, 100, or at least 150 consecutive nucleotides of the disclosed nucleic acid sequences. Probes and primers may be considerably longer than these examples, and it is understood that any length supported by the specification, including the tables, figures, and Sequence Listing, may be used.

Methods for preparing and using probes and primers are described in the references, for

35

example Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, 2nd ed., vol. 1-3, Cold Spring Harbor Press, Plainview NY; Ausubel, F.M. et al., 1987, Current Protocols in Molecular Biology, Greene Publ. Assoc. & Wiley-Intersciences, New York NY; Innis, M. et al., 1990, PCR Protocols, A Guide to Methods and Applications, Academic Press, San Diego CA. PCR primer pairs can be derived from a known sequence, for example, by using computer programs intended for that purpose such as Primer (Version 0.5, 1991, Whitehead Institute for Biomedical Research, Cambridge MA).

Oligonucleotides for use as primers are selected using software known in the art for such purpose. For example, OLIGO 4.06 software is useful for the selection of PCR primer pairs of up to 10 100 nucleotides each, and for the analysis of oligonucleotides and larger polynucleotides of up to 5,000 nucleotides from an input polynucleotide sequence of up to 32 kilobases. Similar primer selection programs have incorporated additional features for expanded capabilities. For example, the PrimOU primer selection program (available to the public from the Genome Center at University of Texas South West Medical Center, Dallas TX) is capable of choosing specific primers from megabase sequences 15 and is thus useful for designing primers on a genome-wide scope. The Primer3 primer selection program (available to the public from the Whitehead Institute/MIT Center for Genome Research, Cambridge MA) allows the user to input a "mispriming library," in which sequences to avoid as primer binding sites are user-specified. Primer3 is useful, in particular, for the selection of oligonucleotides for microarrays. (The source code for the latter two primer selection programs may also be obtained from 20 their respective sources and modified to meet the user's specific needs.) The PrimeGen program (available to the public from the UK Human Genome Mapping Project Resource Centre, Cambridge UK) designs primers based on multiple sequence alignments, thereby allowing selection of primers that hybridize to either the most conserved or least conserved regions of aligned nucleic acid sequences. Hence, this program is useful for identification of both unique and conserved oligonucleotides and 25 polynucleotide fragments. The oligonucleotides and polynucleotide fragments identified by any of the above selection methods are useful in hybridization technologies, for example, as PCR or sequencing primers, microarray elements, or specific probes to identify fully or partially complementary polynucleotides in a sample of nucleic acids. Methods of oligonucleotide selection are not limited to those described above.

A "recombinant nucleic acid" is a sequence that is not naturally occurring or has a sequence that is made by an artificial combination of two or more otherwise separated segments of sequence.

This artificial combination is often accomplished by chemical synthesis or, more commonly, by the artificial manipulation of isolated segments of nucleic acids, e.g., by genetic engineering techniques such as those described in Sambrook, suppra. The term recombinant includes nucleic acids that have been altered solely by addition, substitution, or deletion of a portion of the nucleic acid. Frequently, a

recombinant nucleic acid may include a nucleic acid sequence operably linked to a promoter sequence. Such a recombinant nucleic acid may be part of a vector that is used, for example, to transform a cell.

Alternatively, such recombinant nucleic acids may be part of a viral vector, e.g., based on a vaccinia virus, that could be use to vaccinate a mammal wherein the recombinant nucleic acid is expressed, inducing a protective immunological response in the mammal.

A "regulatory element" refers to a nucleic acid sequence usually derived from untranslated regions of a gene and includes enhancers, promoters, introns, and 5' and 3' untranslated regions (UTRs). Regulatory elements interact with host or viral proteins which control transcription, translation, or RNA stability.

"Reporter molecules" are chemical or biochemical moieties used for labeling a nucleic acid, amino acid, or antibody. Reporter molecules include radionuclides; enzymes; fluorescent, chemiluminescent, or chromogenic agents; substrates; cofactors; inhibitors; magnetic particles; and other moieties known in the art.

An "RNA equivalent," in reference to a DNA sequence, is composed of the same linear sequence of nucleotides as the reference DNA sequence with the exception that all occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose.

The term "sample" is used in its broadest sense. A sample suspected of containing nucleic acids encoding GBAP, or fragments thereof, or GBAP itself, may comprise a bodily fluid; an extract 20 from a cell, chromosome, organelle, or membrane isolated from a cell; a cell; genomic DNA, RNA, or cDNA, in solution or bound to a substrate; a tissue; a tissue print; etc.

The terms "specific binding" and "specifically binding" refer to that interaction between a protein or peptide and an agonist, an antibody, an antagonist, a small molecule, or any natural or synthetic binding composition. The interaction is dependent upon the presence of a particular structure of the protein, e.g., the antigenic determinant or epitope, recognized by the binding molecule. For example, if an antibody is specific for epitope "A," the presence of a polypeptide comprising the epitope A, or the presence of free unlabeled A, in a reaction containing free labeled A and the antibody will reduce the amount of labeled A that binds to the antibody.

The term "substantially purified" refers to nucleic acid or amino acid sequences that are removed from their natural environment and are isolated or separated, and are at least 60% free, preferably at least 75% free, and most preferably at least 90% free from other components with which they are naturally associated.

A "substitution" refers to the replacement of one or more amino acid residues or nucleotides by different amino acid residues or nucleotides, respectively.

"Substrate" refers to any suitable rigid or semi-rigid support including membranes, filters,

chips, slides, wafers, fibers, magnetic or nonmagnetic beads, gels, tubing, plates, polymers, microparticles and capillaries. The substrate can have a variety of surface forms, such as wells, trenches, pins, channels and pores, to which polynucleotides or polypeptides are bound.

A "transcript image" refers to the collective pattern of gene expression by a particular cell type 5 or tissue under given conditions at a given time.

"Transformation" describes a process by which exogenous DNA is introduced into a recipient cell. Transformation may occur under natural or artificial conditions according to various methods well known in the art, and may rely on any known method for the insertion of foreign nucleic acid sequences into a prokaryotic or eukaryotic host cell. The method for transformation is selected based on the type of host cell being transformed and may include, but is not limited to, bacteriophage or viral infection, electroporation, heat shock, lipofection, and particle bombardment. The term "transformed" cells includes stably transformed cells in which the inserted DNA is capable of replication either as an autonomously replicating plasmid or as part of the host chromosome, as well as transiently transformed cells which express the inserted DNA or RNA for limited periods of time.

A "transgenic organism," as used herein, is any organism, including but not limited to animals and plants, in which one or more of the cells of the organism contains heterologous nucleic acid introduced by way of human intervention, such as by transgenic techniques well known in the art. The nucleic acid is introduced into the cell, directly or indirectly by introduction into a precursor of the cell, by way of deliberate genetic manipulation, such as by microinjection or by infection with a recombinant virus. The term genetic manipulation does not include classical cross-breeding, or in vitro fertilization, but rather is directed to the introduction of a recombinant DNA molecule. The transgenic organisms contemplated in accordance with the present invention include bacteria, cyanobacteria, fungi, plants, and animals. The isolated DNA of the present invention can be introduced into the host by methods known in the art, for example infection, transfection,

25 transformation or transconjugation. Techniques for transferring the DNA of the present invention into such organisms are widely known and provided in references such as Sambrook et al. (1989), supra.

A "variant" of a particular nucleic acid sequence is defined as a nucleic acid sequence having at least 40% sequence identity to the particular nucleic acid sequence over a certain length of one of the nucleic acid sequences using blastn with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of nucleic acids may show, for example, at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95% or at least 98% or greater sequence identity over a certain defined length. A variant may be described as, for example, an "allelic" (as defined above), "splice," "species," or "polymorphic" variant. A splice variant may have significant identity to a reference molecule, but will generally have a greater or lesser number of polynucleotides

due to alternative splicing of exons during mRNA processing. The corresponding polypeptide may possess additional functional domains or lack domains that are present in the reference molecule. Species variants are polynucleotide sequences that vary from one species to another. The resulting polypeptides generally will have significant amino acid identity relative to each other. A polymorphic variant is a variation in the polynucleotide sequence of a particular gene between individuals of a given species. Polymorphic variants also may encompass "single nucleotide polymorphisms" (SNPs) in which the polynucleotide sequence varies by one nucleotide base. The presence of SNPs may be indicative of, for example, a certain population, a disease state, or a propensity for a disease state.

A "variant" of a particular polypeptide sequence is defined as a polypeptide sequence having at least 40% sequence identity to the particular polypeptide sequence over a certain length of one of the polypeptide sequences using blastp with the "BLAST 2 Sequences" tool Version 2.0.9 (May-07-1999) set at default parameters. Such a pair of polypeptides may show, for example, at least 50%, at least 50%, at least 90%, at least 95%, or at least 98% or greater sequence identity over a certain defined length of one of the polypeptides.

15 THE INVENTION

The invention is based on the discovery of new human GTP-binding associated proteins (GBAP), the polynucleotides encoding GBAP, and the use of these compositions for the diagnosis, treatment, or prevention of immune system, reproductive, nervous system, and cell signaling disorders, and cell proliferative disorders including cance.

- Table 1 lists the Incyte clones used to assemble full length nucleotide sequences encoding GBAP. Columns 1 and 2 show the sequence identification numbers (SEQ ID NOs) of the polypeptide and nucleotide sequences, respectively. Column 3 shows the clone IDs of the Incyte clones in which nucleic acids encoding each GBAP were identified, and column 4 shows the cDNA libraries from which these clones were isolated. Column 5 shows Incyte clones and their corresponding cDNA libraries.
- 25 Clones for which cDNA libraries are not indicated were derived from pooled cDNA libraries. In some cases, GenBank sequence identifiers are also shown in column 5. The Incyte clones and GenBank cDNA sequences, where indicated, in column 5 were used to assemble the consensus nucleotide sequence of each GBAP and are useful as fragments in hybridization technologies.
- The columns of Table 2 show various properties of each of the polypeptides of the invention:

 30 column 1 references the SEQ ID NO; column 2 shows the number of amino acid residues in each polypeptide; column 3 shows potential phosphorylation sites; column 4 shows potential glycosylation sites; column 5 shows the amino acid residues comprising signature sequences and motifs; column 6 shows homologous sequences as identified by BLAST analysis; and column 7 shows analytical methods and in some cases, searchable databases to which the analytical methods were applied. The methods of column 7 were used to characterize each polypeptide through sequence homology and protein motifs.

The columns of Table 3 show the tissue-specificity and diseases, disorders, or conditions associated with nucleotide sequences encoding GBAP. The first column of Table 3 lists the nucleotide SEQ ID NOs. Column 2 lists fragments of the nucleotide sequences of column 1. These fragments are useful, for example, in hybridization or amplification technologies to identify SEQ ID NO:67-132 and 5 to distinguish between SEQ ID NO:67-132 and related polynucleotide sequences. The polypeptides encoded by these fragments are useful, for example, as immunogenic peptides. Column 3 lists tissue categories which express GBAP as a fraction of total tissues expressing GBAP. Column 4 lists diseases, disorders, or conditions associated with those tissues expressing GBAP as a fraction of total tissues expressing GBAP. Column 5 lists the vectors used to subclone each cDNA library. Of particular note is the expression of SEQ ID NO:84 in lung tissues, and the tissue-specific expression of SEQ ID NO:132. Over 90% of tissues expressing SEQ ID NO:132 are derived from the nervous system, particularly the brain.

The columns of Table 4 show descriptions of the tissues used to construct the cDNA libraries from which cDNA clones encoding GBAP were isolated. Column 1 references the nucleotide SEQ ID NOs, column 2 shows the cDNA libraries from which these clones were isolated, and column 3 shows the tissue origins and other descriptive information relevant to the cDNA libraries in column 2.

SEQ ID NO:70 maps to chromosome 7 within the interval from 111.6 to 123.4 centiMorgans. This interval contains a gene that is down regulated in adenoma. SEQ ID NO:74 maps to chromosome 11 within the interval from 104.8 to 123.5 centiMorgans. This interval contains a gene associated with 20 the cerebellar degenerative disorder, ataxia telangiectasia. SEQ ID NO:75 maps to chromosome 17 within the interval from 62.9 to 65.0 centiMorgans. SEQ ID NO:77 maps to chromosome 3 within the interval from 12.9 to 16.5 centiMorgans. SEQ ID NO:80 maps to chromosome 9 within the interval from 42.0 to 57.3 centiMorgans. SEQ ID NO:86 maps to chromosome 1 within the interval from 159.6 to 164.1 centiMorgans. SEQ ID NO:87 maps to chromosome 11 within the interval from 147.2 to 25 151.6. SEQ ID NO:90 maps to chromosome 1 within the interval from 219.2 to 223.0 centiMorgans. This interval contains a gene encoding a RAB interacting protein. SEQ ID NO:92 and SEQ ID NO:106 both map to chromosome 1 within the interval from 48.8 to 81.6 centiMorgans. This interval also contains genes associated with familial hypercholesterolemia, glucose transport defect, infantile hypophosphatasia, infantile neuronal ceroid lipofuscinosis, Kostmann disease, multiple epiphyseal 30 dysplasia, porphyria cutanea tarda, and T-cell acute lymphocytic leukemia 1. SEQ ID NO:93 maps to chromosome 12 within the interval from 76.5 to 87.6 centiMorgans. This interval also contains genes associated with mucopolysaccharidosis type IIID, pseudovitamin D deficiency rickets, and renal amyloidosis. SEQ ID NO:94 and SEQ ID NO:109 both map to chromosome 1 within the interval from 143.1 to 146.6 centiMorgans, to chromosome 14 within the interval from 46.8 to 50.9 centiMorgans, to 35 chromosome 16 within the interval from 88.1 to 90.2 centiMorgans, and to chromosome 19 within the

interval from 58.7 to 97.5 centiMorgans. The interval on chromosome 14 from 46.8 to 50.9 centiMorgans also contains a gene associated with dopa-responsive dystonia. The interval on chromosome 19 from 58.7 to 97.5 centiMorgans also contains genes associated with colorectal cancer, DNA ligase I deficiency, glutaricaciduria IIB, myotonic dystrophy, renal amyloidosis, T-cell acute 5 lymphoblastic leukemia, and xeroderma pigmentosum D. SEQ ID NO:97 maps to chromosome 2 within the interval from 236.2 to 269.5 centiMorgans. This interval also contains genes associated with Crigler-Najjar syndrome, familial hypercholesterolemia, Oguchi disease, and primary hyperoxaluria. SEQ ID NO:101 maps to chromosome 2 within the interval from 225.6 to 233.1 centiMorgans, to chromosome 6 within the interval from 132.7 to 144.4 centiMorgans, and to chromosome 11 within the 10 interval from 117.9 to 120.8 centiMorgans. The interval on chromosome 2 from 225.6 to 233.1 centiMorgans also contains a gene associated with Waardenburg syndrome 1. The interval on chromosome 6 from 132.7 to 144.4 centiMorgans also contains genes associated with familial disseminated atypical mycobacterial infection and rhizomelic chondrodysplasia punctata. The interval on chromosome 11 from 117.9 to 120.8 centiMorgans also contains a gene associated with acute 15 intermittent porphyria. SEQ ID NO:111 maps to chromosome 19 within the interval from 35.5 to 49.4 centiMorgans, to chromosome 1 within the interval from the p-terminus to 16.4 centiMorgans, and to chromosome 11 within the interval from 147.2 centiMorgans to the q-terminus. SEQ ID NO:112 maps to chromosome 19 within the interval from 41.7 to 49.4 centiMorgans. SEQ ID NO:113 maps to chromosome 9 within the interval from 136.2 to 163.0 centiMorgans. SEQ ID NO:115 maps to 20 chromosome 14 within the interval from 95.5 to 103.7 centiMorgans and to the X chromosome (23) within the interval from the p-terminus to 55.5 centiMorgans. SEQ ID NO:117 maps to chromosome 13 at 46.9 centiMorgans. SEQ ID NO:118 maps to chromosome 1 within the interval from 16.4 to 22.9 centiMorgans. SEQ ID NO:121 maps to chromosome 12 within the interval from 116.6 to 118.9 centiMorgans. SEQ ID NO:128 maps to chromosome 1 within the interval from the p-terminus to 16.4 25 centiMorgans.

The invention also encompasses GBAP variants. A preferred GBAP variant is one which has at least about 80%, or alternatively at least about 90%, or even at least about 95% amino acid sequence identity to the GBAP amino acid sequence, and which contains at least one functional or structural characteristic of GBAP.

The invention also encompasses polynucleotides which encode GBAP. In a particular embodiment, the invention encompasses a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:67-132, which encodes GBAP. The polynucleotide sequences of SEQ ID NO:67-132, as presented in the Sequence Listing, embrace the equivalent RNA sequences, wherein occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose.

The invention also encompasses a variant of a polynucleotide sequence encoding GBAP. In particular, such a variant polynucleotide sequence will have at least about 70%, or alternatively at least about 85%, or even at least about 95% polynucleotide sequence identity to the polynucleotide sequence encoding GBAP. A particular aspect of the invention encompasses a variant of a polynucleotide sequence comprising a sequence selected from the group consisting of SEQ ID NO:67-132 which has at least about 70%, or alternatively at least about 85%, or even at least about 95% polynucleotide sequence identity to a nucleic acid sequence selected from the group consisting of SEQ ID NO:67-132. Any one of the polynucleotide variants described above can encode an amino acid sequence which contains at least one functional or structural characteristic of GBAP.

It will be appreciated by those skilled in the art that as a result of the degeneracy of the genetic code, a multitude of polynucleotide sequences encoding GBAP, some bearing minimal similarity to the polynucleotide sequences of any known and naturally occurring gene, may be produced. Thus, the invention contemplates each and every possible variation of polynucleotide sequence that could be made by selecting combinations based on possible codon choices. These combinations are made in

15 accordance with the standard triplet genetic code as applied to the polynucleotide sequence of naturally occurring GBAP, and all such variations are to be considered as being specifically disclosed.

Although nucleotide sequences which encode GBAP and its variants are generally capable of hybridizing to the nucleotide sequence of the naturally occurring GBAP under appropriately selected conditions of stringency, it may be advantageous to produce nucleotide sequences encoding GBAP or its derivatives possessing a substantially different codon usage, e.g., inclusion of non-naturally occurring codons. Codons may be selected to increase the rate at which expression of the peptide occurs in a particular prokaryotic or eukaryotic host in accordance with the frequency with which particular codons are utilized by the host. Other reasons for substantially altering the nucleotide sequence encoding GBAP and its derivatives without altering the encoded amino acid sequences include the production of RNA transcripts having more desirable properties, such as a greater half-life, than transcripts produced from the naturally occurring sequence.

The invention also encompasses production of DNA sequences which encode GBAP and GBAP derivatives, or fragments thereof, entirely by synthetic chemistry. After production, the synthetic sequence may be inserted into any of the many available expression vectors and cell systems using reagents well known in the art. Moreover, synthetic chemistry may be used to introduce mutations into a sequence encoding GBAP or any fragment thereof.

Also encompassed by the invention are polynucleotide sequences that are capable of hybridizing to the claimed polynucleotide sequences, and, in particular, to those shown in SEQ ID NO:67-132 and fragments thereof under various conditions of stringency. (See, e.g., Wahl, G.M. and S.L. Berger (1987) Methods Enzymol. 152:399-407; Kimmel, A.R. (1987) Methods Enzymol.

152:507-511.) Hybridization conditions, including annealing and wash conditions, are described in "Definitions."

Methods for DNA sequencing are well known in the art and may be used to practice any of the embodiments of the invention. The methods may employ such enzymes as the Klenow fragment of DNA polymerase I, SEQUENASE (US Biochemical, Cleveland OH), Taq polymerase (PE Biosystems, Foster City CA), thermostable T7 polymerase (Amersham Pharmacia Biotech, Piscataway NJ), or combinations of polymerases and proofreading exonucleases such as those found in the ELONGASE amplification system (Life Technologies, Gaithersburg MD). Preferably, sequence preparation is automated with machines such as the MICROLAB 2200 liquid transfer system (Hamilton, Reno NV), PTC200 thermal cycler (MJ Research, Watertown MA) and ABI CATALYST 800 thermal cycler (PE Biosystems). Sequencing is then carried out using either the ABI 373 or 377 DNA sequencing system (PE Biosystems), the MEGABACE 1000 DNA sequencing system (Molecular Dynamics, Sunnyvale CA), or other systems known in the art. The resulting sequences are analyzed using a variety of algorithms which are well known in the art. (See, e.g., Ausubel, F.M. (1997) Short Protocols in Molecular Biology, John Wiley & Sons, New York NY, unit 7.7; Meyers, R.A. (1995) Molecular Biology and Biotechnology, Wiley VCH, New York NY, pp. 856-853.)

The nucleic acid sequences encoding GBAP may be extended utilizing a partial nucleotide sequence and employing various PCR-based methods known in the art to detect upstream sequences. such as promoters and regulatory elements. For example, one method which may be employed, 20 restriction-site PCR, uses universal and nested primers to amplify unknown sequence from genomic DNA within a cloning vector. (See, e.g., Sarkar, G. (1993) PCR Methods Applic. 2:318-322.) Another method, inverse PCR, uses primers that extend in divergent directions to amplify unknown sequence from a circularized template. The template is derived from restriction fragments comprising a known genomic locus and surrounding sequences. (See, e.g., Triglia, T. et al. (1988) Nucleic Acids 25 Res. 16:8186.) A third method, capture PCR, involves PCR amplification of DNA fragments adjacent to known sequences in human and yeast artificial chromosome DNA. (See, e.g., Lagerstrom, M. et al. (1991) PCR Methods Applic. 1:111-119.) In this method, multiple restriction enzyme digestions and ligations may be used to insert an engineered double-stranded sequence into a region of unknown sequence before performing PCR. Other methods which may be used to retrieve unknown sequences 30 are known in the art. (See, e.g., Parker, J.D. et al. (1991) Nucleic Acids Res. 19:3055-3060). Additionally, one may use PCR, nested primers, and PROMOTERFINDER libraries (Clontech, Palo Alto CA) to walk genomic DNA. This procedure avoids the need to screen libraries and is useful in finding intron/exon junctions. For all PCR-based methods, primers may be designed using commercially available software, such as OLIGO 4.06 Primer Analysis software (National Biosciences, 35 Plymouth MN) or another appropriate program, to be about 22 to 30 nucleotides in length, to have a

GC content of about 50% or more, and to anneal to the template at temperatures of about 68°C to 72°C.

When screening for full-length cDNAs, it is preferable to use libraries that have been size-selected to include larger cDNAs. In addition, random-primed libraries, which often include sequences containing the 5' regions of genes, are preferable for situations in which an oligo d(T) library does not yield a full-length cDNA. Genomic libraries may be useful for extension of sequence into 5' non-transcribed regulatory regions.

Capillary electrophoresis systems which are commercially available may be used to analyze the size or confirm the nucleotide sequence of sequencing or PCR products. In particular, capillary sequencing may employ flowable polymers for electrophoretic separation, four different nucleotide-specific, laser-stimulated fluorescent dyes, and a charge coupled device camera for detection of the emitted wavelengths. Output/light intensity may be converted to electrical signal using appropriate software (e.g., GENOTYPER and SEQUENCE NAVIGATOR, PE Biosystems), and the entire process from loading of samples to computer analysis and electronic data display may be computer controlled. Capillary electrophoresis is especially preferable for sequencing small DNA fragments which may be present in limited amounts in a particular sample.

In another embodiment of the invention, polynucleotide sequences or fragments thereof which encode GBAP may be cloned in recombinant DNA molecules that direct expression of GBAP, or fragments or functional equivalents thereof, in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be produced and used to express GBAP.

The nucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter GBAP-encoding sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. For example, oligonucleotide-mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth.

The nucleotides of the present invention may be subjected to DNA shuffling techniques such as MOLECULARBREEDING (Maxygen Inc., Santa Clara CA; described in U.S. Patent Number 5,837,458; Chang, C.-C. et al. (1999) Nat. Biotechnol. 17:793-797; Christians, F.C. et al. (1999) Nat. Biotechnol. 17:259-264; and Crameri, A. et al. (1996) Nat. Biotechnol. 14:315-319) to alter or improve the biological properties of GBAP, such as its biological or enzymatic activity or its ability to bind to other molecules or compounds. DNA shuffling is a process by which a library of gene variants is produced using PCR-mediated recombination of gene fragments. The library is then

PCT/US00/19698 **WO** 01/05970

subjected to selection or screening procedures that identify those gene variants with the desired properties. These preferred variants may then be pooled and further subjected to recursive rounds of DNA shuffling and selection/screening. Thus, genetic diversity is created through "artificial" breeding and rapid molecular evolution. For example, fragments of a single gene containing random 5 point mutations may be recombined, screened, and then reshuffled until the desired properties are optimized. Alternatively, fragments of a given gene may be recombined with fragments of homologous genes in the same gene family, either from the same or different species, thereby maximizing the genetic diversity of multiple naturally occurring genes in a directed and controllable manner.

In another embodiment, sequences encoding GBAP may be synthesized, in whole or in part, 10 using chemical methods well known in the art. (See, e.g., Caruthers, M.H. et al. (1980) Nucleic Acids Symp. Ser. 7:215-223; and Horn, T. et al. (1980) Nucleic Acids Symp. Ser. 7:225-232.) Alternatively, GBAP itself or a fragment thereof may be synthesized using chemical methods. For example, peptide synthesis can be performed using various solution-phase or solid-phase techniques. (See, e.g., 15 Creighton, T. (1984) Proteins, Structures and Molecular Properties, WH Freeman, New York NY, pp. 55-60; and Roberge, J.Y. et al. (1995) Science 269:202-204.) Automated synthesis may be achieved using the ABI 431A peptide synthesizer (PE Biosystems). Additionally, the amino acid sequence of GBAP, or any part thereof, may be altered during direct synthesis and/or combined with sequences from other proteins, or any part thereof, to produce a variant polypeptide or a polypeptide having a 20 sequence of a naturally occurring polypeptide.

The peptide may be substantially purified by preparative high performance liquid chromatography. (See, e.g., Chiez, R.M. and F.Z. Regnier (1990) Methods Enzymol. 182:392-421.) The composition of the synthetic peptides may be confirmed by amino acid analysis or by sequencing. (See, e.g., Creighton, supra, pp. 28-53.)

25

In order to express a biologically active GBAP, the nucleotide sequences encoding GBAP or derivatives thereof may be inserted into an appropriate expression vector, i.e., a vector which contains the necessary elements for transcriptional and translational control of the inserted coding sequence in a suitable host. These elements include regulatory sequences, such as enhancers, constitutive and inducible promoters, and 5' and 3' untranslated regions in the vector and in polynucleotide sequences 30 encoding GBAP. Such elements may vary in their strength and specificity. Specific initiation signals may also be used to achieve more efficient translation of sequences encoding GBAP. Such signals include the ATG initiation codon and adjacent sequences, e.g. the Kozak sequence. In cases where sequences encoding GBAP and its initiation codon and upstream regulatory sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be 35 needed. However, in cases where only coding sequence, or a fragment thereof, is inserted, exogenous

translational control signals including an in-frame ATG initiation codon should be provided by the vector. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate for the particular host cell system used. (See, e.g., Scharf, D. et al. (1994) Results Probl. Cell Differ. 5 20:125-162.)

Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding GBAP and appropriate transcriptional and translational control elements. These methods include <u>in vitro</u> recombinant DNA techniques, synthetic techniques, and <u>in vivo</u> genetic recombination. (See, e.g., Sambrook, J. et al. (1989) <u>Molecular Cloning, A Laboratory</u>

10 <u>Manual</u>, Cold Spring Harbor Press, Plainview NY, ch. 4, 8, and 16-17; Ausubel, F.M. et al. (1995)

<u>Current Protocols in Molecular Biology</u>, John Wiley & Sons, New York NY, ch. 9, 13, and 16.)

A variety of expression vector/host systems may be utilized to contain and express sequences encoding GBAP. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with 15 yeast expression vectors; insect cell systems infected with viral expression vectors (e.g., baculovirus); plant cell systems transformed with viral expression vectors (e.g., cauliflower mosaic virus, CaMV, or tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems. (See, e.g., Sambrook, supra; Ausubel, supra; Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509; Bitter, G.A. et al. (1987) Methods Enzymol. 153:516-544; 20 Scorer, C.A. et al. (1994) Bio/Technology 12:181-184; Engelhard, E.K. et al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945; Takamatsu, N. (1987) EMBO J. 6:307-311; Coruzzi, G. et al. (1984) EMBO J. 3:1671-1680; Broglie, R. et al. (1984) Science 224:838-843; Winter, J. et al. (1991) Results Probl. Cell Differ. 17:85-105; The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 25 191-196; Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. USA 81:3655-3659; and Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355.) Expression vectors derived from retroviruses, adenoviruses, or herpes or vaccinia viruses, or from various bacterial plasmids; may be used for delivery of nucleotide sequences to the targeted organ, tissue, or cell population. (Scc, e.g., Di Nicola, M. et al. (1998) Cancer Gen. Ther. 5(6):350-356; Yu, M. et al., (1993) Proc. Natl. Acad. Sci. 30 USA 90(13):6340-6344; Buller, R.M. et al. (1985) Nature 317(6040):813-815; McGregor, D.P. et al. (1994) Mol. Immunol. 31(3):219-226; and Verma, I.M. and N. Somia (1997) Nature 389:239-242.) The invention is not limited by the host cell employed.

In bacterial systems, a number of cloning and expression vectors may be selected depending upon the use intended for polynucleotide sequences encoding GBAP. For example, routine cloning, subcloning, and propagation of polynucleotide sequences encoding GBAP can be achieved using a

multifunctional E. coli vector such as PBLUESCRIPT (Stratagene, La Jolla CA) or PSPORT1 plasmid (Life Technologies). Ligation of sequences encoding GBAP into the vector's multiple cloning site disrupts the lacZ gene, allowing a colorimetric screening procedure for identification of transformed bacteria containing recombinant molecules. In addition, these vectors may be useful for in vitro 5 transcription, dideoxy sequencing, single strand rescue with helper phage, and creation of nested deletions in the cloned sequence. (See, e.g., Van Heeke, G. and S.M. Schuster (1989) J. Biol. Chem. 264:5503-5509.) When large quantities of GBAP are needed, e.g. for the production of antibodies, vectors which direct high level expression of GBAP may be used. For example, vectors containing the strong, inducible T5 or T7 bacteriophage promoter may be used.

Yeast expression systems may be used for production of GBAP. A number of vectors containing constitutive or inducible promoters, such as alpha factor, alcohol oxidase, and PGH promoters, may be used in the yeast Saccharomyces cerevisiae or Pichia pastoris. In addition, such vectors direct either the secretion or intracellular retention of expressed proteins and enable integration of foreign sequences into the host genome for stable propagation. (See, e.g., Ausubel, 1995, supra; 15 Bitter, supra; and Scorer, supra.)

10

Plant systems may also be used for expression of GBAP. Transcription of sequences encoding GBAP may be driven viral promoters, e.g., the 35S and 19S promoters of CaMV used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) EMBO J. 6:307-311). Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be 20 used. (See, e.g., Coruzzi, supra; Broglie, supra; and Winter, supra.) These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. (See, e.g., The McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York NY, pp. 191-196.)

In mammalian cells, a number of viral-based expression systems may be utilized. In cases 25 where an adenovirus is used as an expression vector, sequences encoding GBAP may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain infective virus which expresses GBAP in host cells. (See, e.g., Logan, J. and T. Shenk (1984) Proc. Natl. Acad. Sci. USA 81:3655-3659.) In addition, transcription enhancers, such as the Rous sarcoma 30 virus (RSV) enhancer, may be used to increase expression in mammalian host cells. SV40 or EBVbased vectors may also be used for high-level protein expression.

Human artificial chromosomes (HACs) may also be employed to deliver larger fragments of DNA than can be contained in and expressed from a plasmid. HACs of about 6 kb to 10 Mb are constructed and delivered via conventional delivery methods (liposomes, polycationic amino polymers, 35 or vesicles) for therapeutic purposes. (See, e.g., Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355.)

For long term production of recombinant proteins in mammalian systems, stable expression of GBAP in cell lines is preferred. For example, sequences encoding GBAP can be transformed into cell lines using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for about 1 to 2 days in enriched media before being switched to selective media. The purpose of the selectable marker is to confer resistance to a selective agent, and its presence allows growth and recovery of cells which successfully express the introduced sequences. Resistant clones of stably transformed cells may be propagated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, 10 but are not limited to, the herpes simplex virus thymidine kinase and adenine phosphoribosyltransferase genes, for use in tk and apr cells, respectively. (See, e.g., Wigler, M. et al. (1977) Cell 11:223-232; Lowy, I. et al. (1980) Cell 22:817-823.) Also, antimetabolite, antibiotic, or herbicide resistance can be used as the basis for selection. For example, dhfr confers resistance to methotrexate; neo confers 15 resistance to the aminoglycosides neomycin and G-418; and als and pat confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively. (See, e.g., Wigler, M. et al. (1980) Proc. Natl. Acad. Sci. USA 77:3567-3570; Colbere-Garapin, F. et al. (1981) J. Mol. Biol. 150:1-14.) Additional selectable genes have been described, e.g., trpB and hisD, which alter cellular requirements for metabolites. (See, e.g., Hartman, S.C. and R.C. Mulligan (1988) Proc. Natl. Acad. Sci. USA 20 85:8047-8051.) Visible markers, e.g., anthocyanins, green fluorescent proteins (GFP; Clontech), B glucuronidase and its substrate B-glucuronide, or luciferase and its substrate luciferin may be used. These markers can be used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system. (See, e.g., Rhodes, C.A. (1995) Methods Mol. Biol. 55:121-131.)

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, the presence and expression of the gene may need to be confirmed. For example, if the sequence encoding GBAP is inserted within a marker gene sequence, transformed cells containing sequences encoding GBAP can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a sequence encoding GBAP under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

In general, host cells that contain the nucleic acid sequence encoding GBAP and that express GBAP may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations, PCR amplification, and protein bioassay or immunoassay techniques which include membrane, solution, or chip based

technologies for the detection and/or quantification of nucleic acid or protein sequences.

Immunological methods for detecting and measuring the expression of GBAP using either specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include enzyme-linked immunosorbent assays (ELISAs), radioimmunoassays (RIAs), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on GBAP is preferred, but a competitive binding assay may be employed. These and other assays are well known in the art. (See, e.g., Hampton, R. et al. (1990) Serological Methods, a Laboratory Manual, APS Press, St. Paul MN, Sect. IV; Coligan, J.E. et al. (1997) Current Protocols in Immunology, Greene Pub. Associates and Wiley-Interscience, New York NY; and Pound, J.D. (1998) Immunochemical Protocols, Humana Press, Totowa NJ.)

A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides encoding GBAP include oligolabeling, nick translation, end-labeling, or PCR amplification using a labeled nucleotide. Alternatively, the sequences encoding GBAP, or any fragments thereof, may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits, such as those provided by Amersham Pharmacia Biotech, Promaga (Madison WI), and US Biochemical. Suitable reporter molecules or labels which may be used for ease of detection include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents, as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with nucleotide sequences encoding GBAP may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a transformed cell may be secreted or retained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides which encode GBAP may be designed to contain signal sequences which direct secretion of GBAP through a prokaryotic or eukaryotic cell membrane.

In addition, a host cell strain may be chosen for its ability to modulate expression of the

30 inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the
polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation,
lipidation, and acylation. Post-translational processing which cleaves a "prepro" or "pro" form of the
protein may also be used to specify protein targeting, folding, and/or activity. Different host cells
which have specific cellular machinery and characteristic mechanisms for post-translational activities

35 (e.g., CHO, HcLa, MDCK, HEK293, and WI38) are available from the American Type Culture

Collection (ATCC, Manassas VA) and may be chosen to ensure the correct modification and processing of the foreign protein.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences encoding GBAP may be ligated to a heterologous sequence resulting in translation of a fusion 5 protein in any of the aforementioned host systems. For example, a chimeric GBAP protein containing a heterologous moiety that can be recognized by a commercially available antibody may facilitate the screening of peptide libraries for inhibitors of GBAP activity. Heterologous protein and peptide moieties may also facilitate purification of fusion proteins using commercially available affinity matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose 10 binding protein (MBP), thioredoxin (Trx), calmodulin binding peptide (CBP), 6-His, FLAG, c-myc, and hemagglutinin (HA). GST, MBP, Trx, CBP, and 6-His enable purification of their cognate fusion proteins on immobilized glutathione, maltose, phenylarsine oxide, calmodulin, and metal-chelate resins, respectively. FLAG, c-myc, and hemagglutinin (HA) enable immunoaffinity purification of fusion proteins using commercially available monoclonal and polyclonal antibodies that specifically recognize 15 these epitope tags. A fusion protein may also be engineered to contain a proteolytic cleavage site located between the GBAP encoding sequence and the heterologous protein sequence, so that GBAP may be cleaved away from the heterologous moiety following purification. Methods for fusion protein expression and purification are discussed in Ausubel (1995, supra, ch. 10). A variety of commercially available kits may also be used to facilitate expression and purification of fusion proteins.

In a further embodiment of the invention, synthesis of radiolabeled GBAP may be achieved <u>in</u> <u>vitro</u> using the TNT rabbit reticulocyte lysate or wheat germ extract system (Promega). These systems couple transcription and translation of protein-coding sequences operably associated with the T7, T3, or SP6 promoters. Translation takes place in the presence of a radiolabeled amino acid precursor, for example, ³⁵S-methionine.

GBAP of the present invention or fragments thereof may be used to screen for compounds that specifically bind to GBAP. At least one and up to a plurality of test compounds may be screened for specific binding to GBAP. Examples of test compounds include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

25

In one embodiment, the compound thus identified is closely related to the natural ligand of GBAP, e.g., a ligand or fragment thereof, a natural substrate, a structural or functional mimetic, or a natural binding partner. (See, Coligan, J.E. et al. (1991) Current Protocols in Immunology 1(2): Chapter 5.) Similarly, the compound can be closely related to the natural receptor to which GBAP binds, or to at least a fragment of the receptor, e.g., the ligand binding site. In either case, the compound can be rationally designed using known techniques. In one embodiment, screening for these compounds involves producing appropriate cells which express GBAP, either as a secreted

protein or on the cell membrane. Preferred cells include cells from mammals, yeast, <u>Drosophila</u>, or <u>E. coli</u>. Cells expressing GBAP or cell membrane fractions which contain GBAP are then contacted with a test compound and binding, stimulation, or inhibition of activity of either GBAP or the compound is analyzed.

An assay may simply test binding of a test compound to the polypeptide, wherein binding is detected by a fluorophore, radioisotope, enzyme conjugate, or other detectable label. For example, the assay may comprise the steps of combining at least one test compound with GBAP, either in solution or affixed to a solid support, and detecting the binding of GBAP to the compound.

Alternatively, the assay may detect or measure binding of a test compound in the presence of a labeled competitor. Additionally, the assay may be carried out using cell-free preparations, chemical libraries, or natural product mixtures, and the test compound(s) may be free in solution or affixed to a solid support.

GBAP of the present invention or fragments thereof may be used to screen for compounds that modulate the activity of GBAP. Such compounds may include agonists, antagonists, or partial or inverse agonists. In one embodiment, an assay is performed under conditions permissive for GBAP activity, wherein GBAP is combined with at least one test compound, and the activity of GBAP in the presence of a test compound is compared with the activity of GBAP in the absence of the test compound. A change in the activity of GBAP in the presence of the test compound is indicative of a compound that modulates the activity of GBAP. Alternatively, a test compound is combined with an in vitro or cell-free system comprising GBAP under conditions suitable for GBAP activity, and the assay is performed. In either of these assays, a test compound which modulates the activity of GBAP may do so indirectly and need not come in direct contact with the test compound. At least one and up to a plurality of test compounds may be screened.

In another embodiment, polynucleotides encoding GBAP or their mammalian homologs may be "knocked out" in an animal model system using homologous recombination in embryonic stem (ES) cells. Such techniques are well known in the art and are useful for the generation of animal models of human disease. (See, e.g., U.S. Patent No. 5,175,383 and U.S. Patent No. 5,767,337.) For example, mouse ES cells, such as the mouse 129/SvJ cell line, are derived from the early mouse embryo and grown in culture. The ES cells are transformed with a vector containing the gene of interest disrupted by a marker gene, e.g., the neomycin phosphotransferase gene (neo; Capecchi, M.R. (1989) Science 244:1288-1292). The vector integrates into the corresponding region of the host genome by homologous recombination. Alternatively, homologous recombination takes place using the Cre-loxP system to knockout a gene of interest in a tissue- or developmental stage-specific manner (Marth, J.D. (1996) Clin. Invest. 97:1999-2002; Wagner, K.U. et al. (1997) Nucleic Acids Res. 25:4323-4330). Transformed ES cells are identified and microinjected into mouse cell blastocysts such as those from the C57BL/6 mouse strain. The blastocysts are surgically transferred

to pseudopregnant dams, and the resulting chimeric progeny are genotyped and bred to produce heterozygous or homozygous strains. Transgenic animals thus generated may be tested with potential therapeutic or toxic agents.

Polynucleotides encoding GBAP may also be manipulated <u>in vitro</u> in ES cells derived from 5 human blastocysts. Human ES cells have the potential to differentiate into at least eight separate cell lineages including endoderm, mesoderm, and ectodermal cell types. These cell lineages differentiate into, for example, neural cells, hematopoietic lineages, and cardiomyocytes (Thomson, J.A. et al. (1998) Science 282:1145-1147).

Polynucleotides encoding GBAP can also be used to create "knockin" humanized animals

10 (pigs) or transgenic animals (mice or rats) to model human disease. With knockin technology, a

region of a polynucleotide encoding GBAP is injected into animal ES cells, and the injected sequence
integrates into the animal cell genome. Transformed cells are injected into blastulae, and the
blastulae are implanted as described above. Transgenic progeny or inbred lines are studied and
treated with potential pharmaceutical agents to obtain information on treatment of a human disease.

15 Alternatively, a mammal inbred to overexpress GBAP, e.g., by secreting GBAP in its milk, may also
serve as a convenient source of that protein (Janne, J. et al. (1998) Biotechnol. Annu. Rev. 4:55-74).

THERAPEUTICS

Chemical and structural similarity, e.g., in the context of sequences and motifs, exists between regions of GBAP and GTP-binding associated proteins. In addition, the expression of GBAP is closely associated with reproductive tissues, inflammation and the immune response, trauma, cell proliferation, and cancer. Therefore, GBAP appears to play a role in immune system, reproductive, nervous system, and cell signaling disorders, and cell proliferative disorders including cancer. In the treatment of disorders associated with increased GBAP expression or activity, it is desirable to decrease the expression or activity of GBAP. In the treatment of disorders associated with decreased GBAP expression or activity, it is desirable to increase the expression or activity of GBAP.

Therefore, in one embodiment, GBAP or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of GBAP. Examples of such disorders include, but are not limited to, an immune system disorder such as inflammation, actinic keratosis, acquired immunodeficiency syndrome (AIDS), 30 Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, arteriosclerosis, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, bursitis, cholecystitis, cirrhosis, contact dermatitis, Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, 435 Hashimoto's thyroiditis, paroxysmal nocturnal hemoglobinuria, hepatitis, hypereosinophilia, irritable

bowel syndrome, episodic lymphopenia with lymphocytotoxins, mixed connective tissue disease (MCTD), multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, myelofibrosis, osteoarthritis, osteoporosis, pancreatitis, polycythemia vera, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, 5 systemic lupus erythematosus, systemic sclerosis, primary thrombocythemia, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, trauma, and hematopoietic cancer including lymphoma, leukemia, and myeloma; a reproductive disorder such as a disorder of prolactin production, infertility, including tubal disease, ovulatory defects, and endometriosis, a disruption of the estrous cycle, a disruption of 10 the menstrual cycle, polycystic ovary syndrome, ovarian hyperstimulation syndrome, an endometrial or ovarian tumor, a uterine fibroid, autoimmune disorders, an ectopic pregnancy, and teratogenesis, cancer of the breast, fibrocystic breast disease, and galactorrhea, a disruption of spermatogenesis, abnormal sperm physiology, cancer of the testis, cancer of the prostate, benign prostatic hyperplasia, prostatitis, Peyronie's disease, impotence, carcinoma of the male breast, and gynecomastia; a nervous 15 system disorder such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural 20 abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases of the nervous system, neurofibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central 25 nervous system, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, endocrine, and toxic myopathies, myasthenia gravis, periodic paralysis, mental disorders including mood, anxiety, and schizophrenic disorders, akathesia, amnesia, catatonia, diabetic neuropathy, 30 tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, and Tourette's disorder; a cell signaling disorder including endocrine disorders such as disorders of the hypothalamus and pituitary resulting from lesions such as primary brain tumors, adenomas, infarction associated with pregnancy, hypophysectomy, aneurysms, vascular malformations, thrombosis, infections, immunological disorders, and complications due to head trauma; disorders associated with 35 hyperpituitarism including acromegaly, giantism, and syndrome of inappropriate antidiuretic hormone

(ADH) secretion (SIADH) often caused by benign adenoma; disorders associated with

hypothyroidism including goiter, myxedema, acute thyroiditis associated with bacterial infection; disorders associated with hyperparathyroidism including Conn disease (chronic hypercalemia); pancreatic disorders such as Type I or Type II diabetes mellitus and associated complications; disorders associated with the adrenals such as hyperplasia, carcinoma, or adenoma of the adrenal 5 cortex, hypertension associated with alkalosis; disorders associated with gonadal steroid hormones such as: in women, abnormal prolactin production, infertility, endometriosis, perturbations of the menstrual cycle, polycystic ovarian disease, hyperprolactinemia, isolated gonadotropin deficiency, amenorrhea, galactorrhea, hermaphroditism, hirsutism and virilization, breast cancer, and, in postmenopausal women, osteoporosis; and, in men, Leydig cell deficiency, male climacteric phase, and 10 germinal cell aplasia, hypergonadal disorders associated with Leydig cell tumors, androgen resistance associated with absence of androgen receptors, syndrome of 5 α-reductase, and gynecomastia; and a cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including 15 adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus.

In another embodiment, a vector capable of expressing GBAP or a fragment or derivative thereof may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of GBAP including, but not limited to, those described above.

In a further embodiment, a pharmaceutical composition comprising a substantially purified GBAP in conjunction with a suitable pharmaceutical carrier may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of GBAP including, but not limited to, those provided above.

In still another embodiment, an agonist which modulates the activity of GBAP may be administered to a subject to treat or prevent a disorder associated with decreased expression or activity of GBAP including, but not limited to, those listed above.

In a further embodiment, an antagonist of GBAP may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of GBAP. Examples of such disorders include, but are not limited to, those immune system, reproductive, nervous system, and cell signaling disorders, and cell proliferative disorders including cancer, described above. In one aspect, an antibody which specifically binds GBAP may be used directly as an antagonist or indirectly as a targeting or delivery mechanism for bringing a pharmaceutical agent to cells or tissues which express GBAP.

PCT/US00/19698 WO 01/05970

In an additional embodiment, a vector expressing the complement of the polynucleotide encoding GBAP may be administered to a subject to treat or prevent a disorder associated with increased expression or activity of GBAP including, but not limited to, those described above.

In other embodiments, any of the proteins, antagonists, antibodies, agonists, complementary 5 sequences, or vectors of the invention may be administered in combination with other appropriate therapeutic agents. Selection of the appropriate agents for use in combination therapy may be made by one of ordinary skill in the art, according to conventional pharmaceutical principles. The combination of therapeutic agents may act synergistically to effect the treatment or prevention of the various disorders described above. Using this approach, one may be able to achieve therapeutic efficacy with 10 lower dosages of each agent, thus reducing the potential for adverse side effects.

An antagonist of GBAP may be produced using methods which are generally known in the art. In particular, purified GBAP may be used to produce antibodies or to screen libraries of pharmaceutical agents to identify those which specifically bind GBAP. Antibodies to GBAP may also be generated using methods that are well known in the art. Such antibodies may include, but are not limited to, 15 polyclonal, monoclonal, chimeric, and single chain antibodies, Fab fragments, and fragments produced by a Fab expression library. Neutralizing antibodies (i.e., those which inhibit dimer formation) are generally preferred for therapeutic use.

For the production of antibodies, various hosts including goats, rabbits, rats, mice, humans, and others may be immunized by injection with GBAP or with any fragment or oligopeptide thereof 20 which has immunogenic properties. Depending on the host species, various adjuvants may be used to increase immunological response. Such adjuvants include, but are not limited to, Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, KLH, and dinitrophenol. Among adjuvants used in humans, BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are especially preferable.

It is preferred that the oligopeptides, peptides, or fragments used to induce antibodies to GBAP have an amino acid sequence consisting of at least about 5 amino acids, and generally will consist of at least about 10 amino acids. It is also preferable that these oligopeptides, peptides, or fragments are identical to a portion of the amino acid sequence of the natural protein. Short stretches of GBAP amino acids may be fused with those of another protein, such as KLH, and antibodies to the chimeric molecule 30 may be produced.

25

Monoclonal antibodies to GBAP may be prepared using any technique which provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-hybridoma technique. (See, e.g., Kohler, G. et al. (1975) Nature 256:495-497; Kozbor, D. et al. (1985) J. 35 Immunol. Methods 81:31-42; Cote, R.J. et al. (1983) Proc. Natl. Acad. Sci. USA 80:2026-2030; and

Cole, S.P. et al. (1984) Mol. Cell Biol. 62:109-120.)

In addition, techniques developed for the production of "chimeric antibodies," such as the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity, can be used. (See, e.g., Morrison, S.L. et al. (1984) Proc.

5 Natl. Acad. Sci. USA 81:6851-6855; Neuberger, M.S. et al. (1984) Nature 312:604-608; and Takeda, S. et al. (1985) Nature 314:452-454.) Alternatively, techniques described for the production of single chain antibodies may be adapted, using methods known in the art, to produce GBAP-specific single chain antibodies. Antibodies with related specificity, but of distinct idiotypic composition, may be generated by chain shuffling from random combinatorial immunoglobulin libraries. (See, e.g., Burton, D.R. (1991) Proc. Natl. Acad. Sci. USA 88:10134-10137.)

Antibodies may also be produced by inducing <u>in vivo</u> production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as disclosed in the literature. (See, e.g., Orlandi, R. et al. (1989) Proc. Natl. Acad. Sci. USA 86:3833-3837; Winter, G. et al. (1991) Nature 349:293-299.)

Antibody fragments which contain specific binding sites for GBAP may also be generated. For example, such fragments include, but are not limited to, F(ab')₂ fragments produced by pepsin digestion of the antibody molecule and Fab fragments generated by reducing the disulfide bridges of the F(ab')₂ fragments. Alternatively, Fab expression libraries may be constructed to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity. (See, e.g., Huse, W.D. et al. (1989) Science 246:1275-1281.)

Various immunoassays may be used for screening to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between GBAP and its specific antibody. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering GBAP epitopes is generally used, but a competitive binding assay may also be employed (Pound, supra).

Various methods such as Scatchard analysis in conjunction with radioimmunoassay techniques may be used to assess the affinity of antibodies for GBAP. Affinity is expressed as an association constant, K_a , which is defined as the molar concentration of GBAP-antibody complex divided by the molar concentrations of free antigen and free antibody under equilibrium conditions. The K_a determined for a preparation of polyclonal antibodies, which are heterogeneous in their affinities for multiple GBAP epitopes, represents the average affinity, or avidity, of the antibodies for GBAP. The K_a determined for a preparation of monoclonal antibodies, which are monospecific for a particular GBAP epitope, represents a true measure of affinity. High-affinity antibody preparations with K_a ranging from

about 10° to 10¹² L/mole are preferred for use in immunoassays in which the GBAP-antibody complex must withstand rigorous manipulations. Low-affinity antibody preparations with K₄ ranging from about 10° to 10⁷ L/mole are preferred for use in immunopurification and similar procedures which ultimately require dissociation of GBAP, preferably in active form, from the antibody (Catty, D. (1988) 5 Antibodies, Volume I: A Practical Approach, IRL Press, Washington DC; Liddell, J.E. and A. Cryer

The titer and avidity of polyclonal antibody preparations may be further evaluated to determine the quality and suitability of such preparations for certain downstream applications. For example, a polyclonal antibody preparation containing at least 1-2 mg specific antibody/ml, preferably 5-10 mg specific antibody/ml, is generally employed in procedures requiring precipitation of GBAP-antibody complexes. Procedures for evaluating antibody specificity, titer, and avidity, and guidelines for antibody quality and usage in various applications, are generally available. (See, e.g., Catty, supra, and Coligan et al., supra.)

(1991) A Practical Guide to Monoclonal Antibodies, John Wiley & Sons, New York NY).

In another embodiment of the invention, the polynucleotides encoding GBAP, or any fragment or complement thereof, may be used for therapeutic purposes. In one aspect, modifications of gene expression can be achieved by designing complementary sequences or antisense molecules (DNA, RNA, PNA, or modified oligonucleotides) to the coding or regulatory regions of the gene encoding GBAP. Such technology is well known in the art, and antisense oligonucleotides or larger fragments can be designed from various locations along the coding or control regions of sequences encoding GBAP.

20 (See, e.g., Agrawal, S., ed. (1996) Antisense Therapeutics, Humana Press Inc., Totawa NJ.)

In therapeutic use, any gene delivery system suitable for introduction of the antisense sequences into appropriate target cells can be used. Antisense sequences can be delivered intracellularly in the form of an expression plasmid which, upon transcription, produces a sequence complementary to at least a portion of the cellular sequence encoding the target protein. (See, e.g.,

- Slater, J.E. et al. (1998) J. Allergy Clin. Immunol. 102(3):469-475; and Scanlon, K.J. et al. (1995) 9(13):1288-1296.) Antisense sequences can also be introduced intracellularly through the use of viral vectors, such as retrovirus and adeno-associated virus vectors. (See, e.g., Miller, A.D. (1990) Blood 76:271; Ausubel, supra; Uckert, W. and W. Walther (1994) Pharmacol. Ther. 63(3):323-347.) Other gene delivery mechanisms include liposome-derived systems, artificial viral envelopes, and other
- 30 systems known in the art. (See, e.g., Rossi, J.J. (1995) Br. Med. Bull. 51(1):217-225; Boado, R.J. et al. (1998) J. Pharm. Sci. 87(11):1308-1315; and Morris, M.C. et al. (1997) Nucleic Acids Res. 25(14):2730-2736.)

In another embodiment of the invention, polynucleotides encoding GBAP may be used for somatic or germline gene therapy. Gene therapy may be performed to (i) correct a genetic deficiency 35 (e.g., in the cases of severe combined immunodeficiency (SCID)-X1 disease characterized by X-linked

inheritance (Cavazzana-Calvo, M. et al. (2000) Science 288:669-672), severe combined immunodeficiency syndrome associated with an inherited adenosine deaminase (ADA) deficiency (Blaese, R.M. et al. (1995) Science 270:475-480; Bordignon, C. et al. (1995) Science 270:470-475), cystic fibrosis (Zabner, J. et al. (1993) Cell 75:207-216; Crystal, R.G. et al. (1995) Hum. Gene Therapy 6:643-666; Crystal, R.G. et al. (1995) Hum. Gene Therapy 6:667-703) shelesception for the

- 5 Therapy 6:643-666; Crystal, R.G. et al. (1995) Hum. Gene Therapy 6:667-703), thalassamias, familial hypercholesterolemia, and hemophilia resulting from Factor VIII or Factor IX deficiencies (Crystal, R.G. (1995) Science 270:404-410; Verma, I.M. and Somia, N. (1997) Nature 389:239-242)), (ii) express a conditionally lethal gene product (e.g., in the case of cancers which result from unregulated cell proliferation), or (iii) express a protein which affords protection against intracellular parasites (e.g.,
- against human retroviruses, such as human immunodeficiency virus (HIV) (Baltimore, D. (1988)
 Nature 335:395-396; Poeschla, E. et al. (1996) Proc. Natl. Acad. Sci. USA. 93:11395-11399),
 hepatitis B or C virus (HBV, HCV); fungal parasites, such as <u>Candida albicans</u> and <u>Paracoccidioides</u>
 <u>brasiliensis</u>; and protozoan parasites such as <u>Plasmodium falciparum</u> and <u>Trypanosoma cruzi</u>). In the case where a genetic deficiency in GBAP expression or regulation causes disease, the expression of
 GBAP from an appropriate population of transduced cells may alleviate the clinical manifestations

caused by the genetic deficiency.

450).

In a further embodiment of the invention, diseases or disorders caused by deficiencies in GBAP are treated by constructing mammalian expression vectors encoding GBAP and introducing these vectors by mechanical means into GBAP-deficient cells. Mechanical transfer technologies for use with cells in vivo or ex vitro include (i) direct DNA microinjection into individual cells, (ii) ballistic gold particle delivery, (iii) liposome-mediated transfection, (iv) receptor-mediated gene transfer, and (v) the use of DNA transposons (Morgan, R.A. and W.F. Anderson (1993) Annu. Rev. Biochem. 62:191-217; Ivics, Z. (1997) Cell 91:501-510; Boulay, J-L. and H. Récipon (1998) Curr. Opin. Biotechnol. 9:445-

Expression vectors that may be effective for the expression of GBAP include, but are not limited to, the PCDNA 3.1, EPITAG, PRCCMV2, PREP, PVAX vectors (Invitrogen, Carlsbad CA), PCMV-SCRIPT, PCMV-TAG, PEGSH/PERV (Stratagene, La Jolla CA), and PTET-OFF, PTET-ON, PTRE2, PTRE2-LUC, PTK-HYG (Clontech, Palo Alto CA). GBAP may be expressed using (i) a constitutively active promoter, (e.g., from cytomegalovirus (CMV), Rous sarcoma virus (RSV), SV40 virus, thymidine kinase (TK), or β-actin genes), (ii) an inducible promoter (e.g., the tetracycline-regulated promoter (Gossen, M. and H. Bujard (1992) Proc. Natl. Acad. Sci. USA 89:5547-5551; Gossen, M. et al. (1995) Science 268:1766-1769; Rossi, F.M.V. and H.M. Blau (1998) Curr. Opin. Biotechnol. 9:451-456), commercially available in the T-REX plasmid (Invitrogen)); the ecdysone-inducible promoter (available in the plasmids PVGRXR and PIND; Invitrogen); the

and H.M. Blau, <u>supra</u>)), or (iii) a tissue-specific promoter or the native promoter of the endogenous gene encoding GBAP from a normal individual.

Commercially available liposome transformation kits (e.g., the PERFECT LIPID TRANSFECTION KIT, available from Invitrogen) allow one with ordinary skill in the art to deliver polynucleotides to target cells in culture and require minimal effort to optimize experimental parameters. In the alternative, transformation is performed using the calcium phosphate method (Graham, F.L. and A.J. Eb (1973) Virology 52:456-467), or by electroporation (Neumann, E. et al. (1982) EMBO J. 1:841-845). The introduction of DNA to primary cells requires modification of these standardized mammalian transfection protocols.

- In another embodiment of the invention, diseases or disorders caused by genetic defects with respect to GBAP expression are treated by constructing a retrovirus vector consisting of (i) the polynucleotide encoding GBAP under the control of an independent promoter or the retrovirus long terminal repeat (LTR) promoter, (ii) appropriate RNA packaging signals, and (iii) a Rev-responsive element (RRE) along with additional retrovirus *cis*-acting RNA sequences and coding sequences required for efficient vector propagation. Retrovirus vectors (c.g., PFB and PFBNEO) are commercially available (Stratagene) and are based on published data (Riviere, I. et al. (1995) Proc. Natl. Acad. Sci. USA 92:6733-6737), incorporated by reference herein. The vector is propagated in an
- receptors on the target cells or a promiscuous envelope protein such as VSVg (Armentano, D. et al. (1987) J. Virol. 61:1647-1650; Bender, M.A. et al. (1987) J. Virol. 61:1639-1646; Adam, M.A. and A.D. Miller (1988) J. Virol. 62:3802-3806; Dull, T. et al. (1998) J. Virol. 72:8463-8471; Zufferey, R. et al. (1998) J. Virol. 72:9873-9880). U.S. Patent Number 5,910,434 to Rigg ("Method for obtaining retrovirus packaging cell lines producing high transducing efficiency retroviral supernatant") discloses a method for obtaining retrovirus packaging cell lines and is hereby incorporated by reference.

appropriate vector producing cell line (VPCL) that expresses an envelope gene with a tropism for

- Propagation of retrovirus vectors, transduction of a population of cells (e.g., CD4* T-cells), and the return of transduced cells to a patient are procedures well known to persons skilled in the art of gene therapy and have been well documented (Ranga, U. et al. (1997) J. Virol. 71:7020-7029; Bauer, G. et al. (1997) Blood 89:2259-2267; Bonyhadi, M.L. (1997) J. Virol. 71:4707-4716; Ranga, U. et al. (1998) Proc. Natl. Acad. Sci. USA 95:1201-1206; Su, L. (1997) Blood 89:2283-2290).
- In the alternative, an adenovirus-based gene therapy delivery system is used to deliver polynucleotides encoding GBAP to cells which have one or more genetic abnormalities with respect to the expression of GBAP. The construction and packaging of adenovirus-based vectors are well known to those with ordinary skill in the art. Replication defective adenovirus vectors have proven to be versatile for importing genes encoding immunoregulatory proteins into intact islets in the pancreas (Csete, M.E. et al. (1995) Transplantation 27:263-268). Potentially useful adenoviral vectors are

described in U.S. Patent Number 5,707,618 to Armentano ("Adenovirus vectors for gene therapy"), hereby incorporated by reference. For adenoviral vectors, see also Antinozzi, P.A. et al. (1999) Annu. Rev. Nutr. 19:511-544; and Verma, I.M. and N. Somia (1997) Nature 18:389:239-242, both incorporated by reference herein.

In another alternative, a herpes-based, gene therapy delivery system is used to deliver 5 polynucleotides encoding GBAP to target cells which have one or more genetic abnormalities with respect to the expression of GBAP. The use of herpes simplex virus (HSV)-based vectors may be especially valuable for introducing GBAP to cells of the central nervous system, for which HSV has a tropism. The construction and packaging of herpes-based vectors are well known to those with 10 ordinary skill in the art. A replication-competent herpes simplex virus (HSV) type 1-based vector has been used to deliver a reporter gene to the eyes of primates (Liu, X. et al. (1999) Exp. Eye Res.169:385-395). The construction of a HSV-1 virus vector has also been disclosed in detail in U.S. Patent Number 5,804,413 to DeLuca ("Herpes simplex virus strains for gene transfer"), which is hereby incorporated by reference. U.S. Patent Number 5,804,413 teaches the use of recombinant HSV 15 d92 which consists of a genome containing at least one exogenous gene to be transferred to a cell under the control of the appropriate promoter for purposes including human gene therapy. Also taught by this patent are the construction and use of recombinant HSV strains deleted for ICP4, ICP27 and ICP22. For HSV vectors, see also Goins, W.F. et al. (1999) J. Virol. 73:519-532 and Xu, H. et al. (1994) Dev. Biol. 163:152-161, hereby incorporated by reference. The manipulation of cloned herpesvirus 20 sequences, the generation of recombinant virus following the transfection of multiple plasmids containing different segments of the large herpesvirus genomes, the growth and propagation of herpesvirus, and the infection of cells with herpesvirus are techniques well known to those of ordinary skill in the art.

In another alternative, an alphavirus (positive, single-stranded RNA virus) vector is used to

deliver polynucleotides encoding GBAP to target cells. The biology of the prototypic alphavirus,

Semliki Forest Virus (SFV), has been studied extensively and gene transfer vectors have been based on
the SFV genome (Garoff, H. and K.-J. Li (1998) Curr. Opin. Biotech. 9:464-469). During alphavirus
RNA replication, a subgenomic RNA is generated that normally encodes the viral capsid proteins. This
subgenomic RNA replicates to higher levels than the full-length genomic RNA, resulting in the
overproduction of capsid proteins relative to the viral proteins with enzymatic activity (e.g., protease
and polymerase). Similarly, inserting the coding sequence for GBAP into the alphavirus genome in
place of the capsid-coding region results in the production of a large number of GBAP-coding RNAs
and the synthesis of high levels of GBAP in vector transduced cells. While alphavirus infection is
typically associated with cell lysis within a few days, the ability to establish a persistent infection in
hamster normal kidney cells (BHK-21) with a variant of Sindbis virus (SIN) indicates that the lytic

replication of alphaviruses can be altered to suit the needs of the gene therapy application (Dryga, S.A. et al. (1997) Virology 228:74-83). The wide host range of alphaviruses will allow the introduction of GBAP into a variety of cell types. The specific transduction of a subset of cells in a population may require the sorting of cells prior to transduction. The methods of manipulating infectious cDNA clones of alphaviruses, performing alphavirus cDNA and RNA transfections, and performing alphavirus infections, are well known to those with ordinary skill in the art.

Oligonucleotides derived from the transcription initiation site, e.g., between about positions -10 and +10 from the start site, may also be employed to inhibit gene expression. Similarly, inhibition can be achieved using triple helix base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or regulatory molecules. Recent therapeutic advances using triplex DNA have been described in the literature. (See, e.g., Gee, J.E. et al. (1994) in Huber, B.E. and B.I. Carr, Molecular and Immunologic Approaches, Futura Publishing, Mt. Kisco NY, pp. 163-177.) A complementary sequence or antisense molecule may also be designed to block translation of mRNA by preventing the transcript from binding to ribosomes.

Ribozymes, enzymatic RNA molecules, may also be used to catalyze the specific cleavage of RNA. The mechanism of ribozyme action involves sequence-specific hybridization of the ribozyme molecule to complementary target RNA, followed by endonucleolytic cleavage. For example, engineered hammerhead motif ribozyme molecules may specifically and efficiently catalyze condonucleolytic cleavage of sequences encoding GBAP.

Specific ribozyme cleavage sites within any potential RNA target are initially identified by scanning the target molecule for ribozyme cleavage sites, including the following sequences: GUA, GUU, and GUC. Once identified, short RNA sequences of between 15 and 20 ribonucleotides, corresponding to the region of the target gene containing the cleavage site, may be evaluated for secondary structural features which may render the oligonucleotide inoperable. The suitability of candidate targets may also be evaluated by testing accessibility to hybridization with complementary oligonucleotides using ribonuclease protection assays.

Complementary ribonucleic acid molecules and ribozymes of the invention may be prepared by any method known in the art for the synthesis of nucleic acid molecules. These include techniques for chemically synthesizing oligonucleotides such as solid phase phosphoramidite chemical synthesis.

Alternatively, RNA molecules may be generated by in vitro and in vivo transcription of DNA sequences encoding GBAP. Such DNA sequences may be incorporated into a wide variety of vectors with suitable RNA polymerase promoters such as T7 or SP6. Alternatively, these cDNA constructs that synthesize complementary RNA, constitutively or inducibly, can be introduced into cell lines, cells, or tissues.

RNA molecules may be modified to increase intracellular stability and half-life. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends of the molecule, or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the backbone of the molecule. This concept is inherent in the production of PNAs and can be extended in all of these molecules by the inclusion of nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, cytidine, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases.

An additional embodiment of the invention encompasses a method for screening for a compound which is effective in altering expression of a polynucleotide encoding GBAP. Compounds which may be effective in altering expression of a specific polynucleotide may include, but are not limited to, oligonucleotides, antisense oligonucleotides, triple helix-forming oligonucleotides, transcription factors and other polypeptide transcriptional regulators, and non-macromolecular chemical entities which are capable of interacting with specific polynucleotide sequences. Effective compounds may alter polynucleotide expression by acting as either inhibitors or promoters of polynucleotide expression. Thus, in the treatment of disorders associated with increased GBAP expression or activity, a compound which specifically inhibits expression of the polynucleotide encoding GBAP may be therapeutically useful, and in the treatment of disorders associated with decreased GBAP expression or activity, a compound which specifically promotes expression of the polynucleotide encoding GBAP may be therapeutically useful.

At least one, and up to a plurality, of test compounds may be screened for effectiveness in 20 altering expression of a specific polynucleotide. A test compound may be obtained by any method commonly known in the art, including chemical modification of a compound known to be effective in altering polynucleotide expression; selection from an existing, commercially-available or proprietary library of naturally-occurring or non-natural chemical compounds; rational design of a compound 25 based on chemical and/or structural properties of the target polynucleotide; and selection from a library of chemical compounds created combinatorially or randomly. A sample comprising a polynucleotide encoding GBAP is exposed to at least one test compound thus obtained. The sample may comprise, for example, an intact or permeabilized cell, or an in vitro cell-free or reconstituted biochemical system. Alterations in the expression of a polynucleotide encoding GBAP are assayed 30 by any method commonly known in the art. Typically, the expression of a specific nucleotide is detected by hybridization with a probe having a nucleotide sequence complementary to the sequence of the polynucleotide encoding GBAP. The amount of hybridization may be quantified, thus forming the basis for a comparison of the expression of the polynucleotide both with and without exposure to one or more test compounds. Detection of a change in the expression of a polynucleotide 35 exposed to a test compound indicates that the test compound is effective in altering the expression of

the polynucleotide. A screen for a compound effective in altering expression of a specific polynucleotide can be carried out, for example, using a Schizosaccharomyces pombe gene expression system (Atkins, D. et al. (1999) U.S. Patent No. 5,932,435; Arndt, G.M. et al. (2000) Nucleic Acids Res. 28:E15) or a human cell line such as HeLa cell (Clarke, M.L. et al. (2000) Biochem. Biophys.

- 5 Res. Commun. 268:8-13). A particular embodiment of the present invention involves screening a combinatorial library of oligonucleotides (such as deoxyribonucleotides, ribonucleotides, peptide nucleic acids, and modified oligonucleotides) for antisense activity against a specific polynucleotide sequence (Bruice, T.W. et al. (1997) U.S. Patent No. 5,686,242; Bruice, T.W. et al. (2000) U.S. Patent No. 6,022,691).
- Many methods for introducing vectors into cells or tissues are available and equally suitable for 10 use in vivo, in vitro, and ex vivo. For ex vivo therapy, vectors may be introduced into stem cells taken from the patient and clonally propagated for autologous transplant back into that same patient. Delivery by transfection, by liposome injections, or by polycationic amino polymers may be achieved using methods which are well known in the art. (See, e.g., Goldman, C.K. et al. (1997) Nat. 15 Biotechnol. 15:462-466.)

Any of the therapeutic methods described above may be applied to any subject in need of such therapy, including, for example, mammals such as humans, dogs, cats, cows, horses, rabbits, and monkeys.

An additional embodiment of the invention relates to the administration of a pharmaceutical 20 composition which generally comprises an active ingredient formulated with a pharmaceutically acceptable excipient. Excipients may include, for example, sugars, starches, celluloses, gums, and proteins. Various formulations are commonly known and are thoroughly discussed in the latest edition of Remington's Pharmaceutical Sciences (Maack Publishing, Easton PA). Such pharmaceutical compositions may consist of GBAP, antibodies to GBAP, and mimetics, agonists, antagonists, or 25 inhibitors of GBAP.

The pharmaceutical compositions utilized in this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, pulmonary, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means.

Pharmaceutical compositions for pulmonary administration may be prepared in liquid or dry powder form. These compositions are generally aerosolized immediately prior to inhalation by the patient. In the case of small molecules (e.g. traditional low molecular weight organic drugs), aerosol delivery of fast-acting formulations is well-known in the art. In the case of macromolecules (e.g. larger peptides and proteins), recent developments in the field of pulmonary delivery via the alveolar region of 35 the lung have enabled the practical delivery of drugs such as insulin to blood circulation (see, e.g.,

30

Patton, J.S. et al., U.S. Patent No. 5,997,848). Pulmonary delivery has the advantage of administration without needle injection, and obviates the need for potentially toxic penetration enhancers.

Pharmaceutical compositions suitable for use in the invention include compositions wherein the active ingredients are contained in an effective amount to achieve the intended purpose. The determination of an effective dose is well within the capability of those skilled in the art.

Specialized forms of pharmaceutical compositions may be prepared for direct intracellular delivery of macromolecules comprising GBAP or fragments thereof. For example, liposome preparations containing a cell-impermeable macromolecule may promote cell fusion and intracellular delivery of the macromolecule. Alternatively, GBAP or a fragment thereof may be joined to a short cationic N-terminal portion from the HIV Tat-1 protein. Fusion proteins thus generated have been found to transduce into the cells of all tissues, including the brain, in a mouse model system (Schwarze, S.R. et al. (1999) Science 285:1569-1572).

For any compound, the therapeutically effective dose can be estimated initially either in cell culture assays, e.g., of neoplastic cells, or in animal models such as mice, rats, rabbits, dogs, monkeys, or pigs. An animal model may also be used to determine the appropriate concentration range and route of administration. Such information can then be used to determine useful doses and routes for administration in humans.

A therapeutically effective dose refers to that amount of active ingredient, for example GBAP or fragments thereof, antibodies of CBAP, and agonists, antagonists or inhibitors of GBAP, which ameliorates the symptoms or condition. Therapeutic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or with experimental animals, such as by calculating the ED₅₀ (the dose therapeutically effective in 50% of the population) or LD₅₀ (the dose lethal to 50% of the population) statistics. The dose ratio of toxic to therapeutic effects is the therapeutic index, which can be expressed as the LD₅₀/ED₅₀ ratio. Pharmaceutical compositions which exhibit large therapeutic indices are preferred. The data obtained from cell culture assays and animal studies are used to formulate a range of dosage for human use. The dosage contained in such compositions is preferably within a range of circulating concentrations that includes the ED₅₀ with little or no toxicity. The dosage varies within this range depending upon the dosage form employed, the sensitivity of the patient, and the route of administration.

The exact dosage will be determined by the practitioner, in light of factors related to the subject requiring treatment. Dosage and administration are adjusted to provide sufficient levels of the active moiety or to maintain the desired effect. Factors which may be taken into account include the severity of the disease state, the general health of the subject, the age, weight, and gender of the subject, time and frequency of administration, drug combination(s), reaction sensitivities, and response to therapy.

35 Long-acting pharmaceutical compositions may be administered every 3 to 4 days, every week, or

30

PCT/US00/19698 WO 01/05970

biweekly depending on the half-life and clearance rate of the particular formulation.

Normal dosage amounts may vary from about 0.1 μ g to 100,000 μ g, up to a total dose of about 1 gram, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature and generally available to practitioners in the art. 5 Those skilled in the art will employ different formulations for nucleotides than for proteins or their inhibitors. Similarly, delivery of polynucleotides or polypeptides will be specific to particular cells, conditions, locations, etc.

DIAGNOSTICS

25

In another embodiment, antibodies which specifically bind GBAP may be used for the diagnosis 10 of disorders characterized by expression of GBAP, or in assays to monitor patients being treated with GBAP or agonists, antagonists, or inhibitors of GBAP. Antibodies useful for diagnostic purposes may be prepared in the same manner as described above for therapeutics. Diagnostic assays for GBAP include methods which utilize the antibody and a label to detect GBAP in human body fluids or in extracts of cells or tissues. The antibodies may be used with or without modification, and may be 15 labeled by covalent or non-covalent attachment of a reporter molecule. A wide variety of reporter molecules, several of which are described above, are known in the art and may be used.

A variety of protocols for measuring GBAP, including ELISAs, RIAs, and FACS, are known in the art and provide a basis for diagnosing altered or abnormal levels of GBAP expression. Normal or standard values for GBAP expression are established by combining body fluids or cell extracts taken 20 from normal mammalian subjects, for example, human subjects, with antibody to GBAP under conditions suitable for complex formation. The amount of standard complex formation may be quantitated by various methods, such as photometric means. Quantities of GBAP expressed in subject, control, and disease samples from biopsied tissues are compared with the standard values. Deviation between standard and subject values establishes the parameters for diagnosing disease.

In another embodiment of the invention, the polynucleotides encoding GBAP may be used for diagnostic purposes. The polynucleotides which may be used include oligonucleotide sequences, complementary RNA and DNA molecules, and PNAs. The polynucleotides may be used to detect and quantify gene expression in biopsied tissues in which expression of GBAP may be correlated with disease. The diagnostic assay may be used to determine absence, presence, and excess expression of 30 GBAP, and to monitor regulation of GBAP levels during therapeutic intervention.

In one aspect, hybridization with PCR probes which are capable of detecting polynucleotide sequences, including genomic sequences, encoding GBAP or closely related molecules may be used to identify nucleic acid sequences which encode GBAP. The specificity of the probe, whether it is made from a highly specific region, e.g., the 5' regulatory region, or from a less specific region, e.g., a 35 conserved motif, and the stringency of the hybridization or amplification will determine whether the

probe identifies only naturally occurring sequences encoding GBAP, allelic variants, or related sequences.

Probes may also be used for the detection of related sequences, and may have at least 50% sequence identity to any of the GBAP encoding sequences. The hybridization probes of the subject invention may be DNA or RNA and may be derived from the sequence of SEQ ID NO:67-132 or from genomic sequences including promoters, enhancers, and introns of the GBAP gene.

Means for producing specific hybridization probes for DNAs encoding GBAP include the cloning of polynucleotide sequences encoding GBAP or GBAP derivatives into vectors for the production of mRNA probes. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by means of the addition of the appropriate RNA polymerases and the appropriate labeled nucleotides. Hybridization probes may be labeled by a variety of reporter groups, for example, by radionuclides such as ³²P or ³⁵S, or by enzymatic labels, such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems, and the like.

Polynucleotide sequences encoding GBAP may be used for the diagnosis of disorders 15 associated with expression of GBAP. Examples of such disorders include, but are not limited to, an immune system disorder such as inflammation, actinic keratosis, acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, ankylosing spondylitis, amyloidosis, anemia, arteriosclerosis, asthma, atherosclerosis, autoimmune hemolytic anemia, autoimmune thyroiditis, bronchitis, bursitis, cholecystitis, cirrhosis, contact dermatitis, 20 Crohn's disease, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, erythroblastosis fetalis, erythema nodosum, atrophic gastritis, glomerulonephritis, Goodpasture's syndrome, gout, Graves' disease, Hashimoto's thyroiditis, paroxysmal nocturnal hemoglobinuria, hepatitis, hypereosinophilia, irritable bowel syndrome, episodic lymphopenia with lymphocytotoxins, mixed connective tissue disease (MCTD), multiple sclerosis, myasthenia gravis, myocardial or pericardial 25 inflammation, myelofibrosis, osteoarthritis, osteoporosis, pancreatitis, polycythemia vcra, polymyositis, psoriasis, Reiter's syndrome, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic anaphylaxis, systemic lupus erythematosus, systemic sclerosis, primary thrombocythemia, thrombocytopenic purpura, ulcerative colitis, uveitis, Werner syndrome, complications of cancer, hemodialysis, and extracorporeal circulation, trauma, and hematopoietic cancer including lymphoma, 30 leukemia, and myeloma; a reproductive disorder such as a disorder of prolactin production, infertility, including tubal disease, ovulatory defects, and endometriosis, a disruption of the estrous cycle, a disruption of the menstrual cycle, polycystic ovary syndrome, ovarian hyperstimulation syndrome, an endometrial or ovarian tumor, a uterine fibroid, autoimmune disorders, an ectopic pregnancy, and teratogenesis, cancer of the breast, fibrocystic breast disease, and galactorrhea, a disruption of 35 spermatogenesis, abnormal sperm physiology, cancer of the testis, cancer of the prostate, benign

prostatic hyperplasia, prostatitis, Peyronie's disease, impotence, carcinoma of the male breast, and gynecomastia; a nervous system disorder such as epilepsy, ischemic cerebrovascular disease, stroke, cerebral neoplasms, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease and other extrapyramidal disorders, amyotrophic lateral sclerosis and other motor neuron 5 disorders, progressive neural muscular atrophy, retinitis pigmentosa, hereditary ataxias, multiple sclerosis and other demyelinating diseases, bacterial and viral meningitis, brain abscess, subdural empyema, epidural abscess, suppurative intracranial thrombophlebitis, myelitis and radiculitis, viral central nervous system disease, prion diseases including kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, fatal familial insomnia, nutritional and metabolic diseases 10 of the nervous system, neurofibromatosis, tuberous sclerosis, cerebelloretinal hemangioblastomatosis, encephalotrigeminal syndrome, mental retardation and other developmental disorders of the central nervous system, cerebral palsy, neuroskeletal disorders, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, dermatomyositis and polymyositis, inherited, metabolic, 15 endocrine, and toxic myopathies, myasthenia gravis, periodic paralysis, mental disorders including mood, anxiety, and schizophrenic disorders, akathesia, amnesia, catatonia, diabetic neuropathy, tardive dyskinesia, dystonias, paranoid psychoses, postherpetic neuralgia, and Tourette's disorder; a cell signaling disorder including endocrine disorders such as disorders of the hypothalamus and pituitary resulting from lesions such as primary brain tumors, adenomas, infarction associated with 20 pregnancy, hypophysectomy, aneurysms, vascular malformations, thrombosis, infections, immunological disorders, and complications due to head trauma; disorders associated with hyperpituitarism including acromegaly, giantism, and syndrome of inappropriate antidiuretic hormone (ADH) secretion (SIADH) often caused by benign adenoma; disorders associated with hypothyroidism including goiter, myxedema, acute thyroiditis associated with bacterial infection; 25 disorders associated with hyperparathyroidism including Conn disease (chronic hypercalemia); pancreatic disorders such as Type I or Type II diabetes mellitus and associated complications; disorders associated with the adrenals such as hyperplasia, carcinoma, or adenoma of the adrenal cortex, hypertension associated with alkalosis; disorders associated with gonadal steroid hormones such as: in women, abnormal prolactin production, infertility, endometriosis, perturbations of the 30 menstrual cycle, polycystic ovarian disease, hyperprolactinemia, isolated gonadotropin deficiency, amenorrhea, galactorrhea, hermaphroditism, hirsutism and virilization, breast cancer, and, in postmenopausal women, osteoporosis; and, in men, Leydig cell deficiency, male climacteric phase, and germinal cell aplasia, hypergonadal disorders associated with Leydig cell tumors, androgen resistance associated with absence of androgen receptors, syndrome of 5 \alpha-reductase, and gynecomastia; and a 35 cell proliferative disorder such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, mixed connective tissue disease (MCTD), myelofibrosis, paroxysmal nocturnal

hemoglobinuria, polycythemia vera, psoriasis, primary thrombocythemia, and cancers including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and, in particular, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus. The polynucleotide sequences encoding GBAP may be used in Southern or northern analysis, dot blot, or other membrane-based technologies; in PCR technologies; in dipstick, pin, and multiformat ELISA-like assays; and in microarrays utilizing fluids or tissues from patients to detect altered GBAP expression. Such qualitative or quantitative methods are well known in the art.

In a particular aspect, the nucleotide sequences encoding GBAP may be useful in assays that detect the presence of associated disorders, particularly those mentioned above. The nucleotide sequences encoding GBAP may be labeled by standard methods and added to a fluid or tissue sample from a patient under conditions suitable for the formation of hybridization complexes. After a suitable incubation period, the sample is washed and the signal is quantified and compared with a standard value. If the amount of signal in the patient sample is significantly altered in comparison to a control sample then the presence of altered levels of nucleotide sequences encoding GBAP in the sample indicates the presence of the associated disorder. Such assays may also be used to evaluate the efficacy of a particular therapeutic treatment regimen in animal studies, in clinical trials, or to monitor the treatment of an individual patient.

In order to provide a basis for the diagnosis of a disorder associated with expression of GBAP, a normal or standard profile for expression is established. This may be accomplished by combining body fluids or cell extracts taken from normal subjects, either animal or human, with a sequence, or a fragment thereof, encoding GBAP, under conditions suitable for hybridization or amplification.

Standard hybridization may be quantified by comparing the values obtained from normal subjects with values from an experiment in which a known amount of a substantially purified polynucleotide is used. Standard values obtained in this manner may be compared with values obtained from samples from patients who are symptomatic for a disorder. Deviation from standard values is used to establish the presence of a disorder.

Once the presence of a disorder is established and a treatment protocol is initiated,

30 hybridization assays may be repeated on a regular basis to determine if the level of expression in the patient begins to approximate that which is observed in the normal subject. The results obtained from successive assays may be used to show the efficacy of treatment over a period ranging from several days to months.

With respect to cancer, the presence of an abnormal amount of transcript (either under- or overexpressed) in biopsied tissue from an individual may indicate a predisposition for the development

of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

- Additional diagnostic uses for oligonucleotides designed from the sequences encoding GBAP may involve the use of PCR. These oligomers may be chemically synthesized, generated enzymatically, or produced in vitro. Oligomers will preferably contain a fragment of a polynucleotide encoding GBAP, or a fragment of a polynucleotide complementary to the polynucleotide encoding GBAP, and will be employed under optimized conditions for identification of a specific gene or condition.
- 10 Oligomers may also be employed under less stringent conditions for detection or quantification of closely related DNA or RNA sequences.

In a particular aspect, oligonucleotide primers derived from the polynucleotide sequences encoding GBAP may be used to detect single nucleotide polymorphisms (SNPs). SNPs are substitutions, insertions and deletions that are a frequent cause of inherited or acquired genetic disease 15 in humans. Methods of SNP detection include, but are not limited to, single-stranded conformation polymorphism (SSCP) and fluorescent SSCP (fSSCP) methods. In SSCP, oligonucleotide primers derived from the polynucleotide sequences encoding GBAP are used to amplify DNA using the polymerase chain reaction (PCR). The DNA may be derived, for example, from diseased or normal tissue, biopsy samples, bodily fluids, and the like. SNPs in the DNA cause differences in the secondary 20 and tertiary structures of PCR products in single-stranded form, and these differences are detectable using gel electrophoresis in non-denaturing gels. In fSCCP, the oligonucleotide primers are fluorescently labeled, which allows detection of the amplimers in high-throughput equipment such as DNA sequencing machines. Additionally, sequence database analysis methods, termed in silico SNP (isSNP), are capable of identifying polymorphisms by comparing the sequence of individual 25 overlapping DNA fragments which assemble into a common consensus sequence. These computerbased methods filter out sequence variations due to laboratory preparation of DNA and sequencing errors using statistical models and automated analyses of DNA sequence chromatograms. In the alternative, SNPs may be detected and characterized by mass spectrometry using, for example, the high throughput MASSARRAY system (Sequenom, Inc., San Diego CA).

Methods which may also be used to quantify the expression of GBAP include radiolabeling or biotinylating nucleotides, coamplification of a control nucleic acid, and interpolating results from standard curves. (See, e.g., Melby, P.C. et al. (1993) J. Immunol. Methods 159:235-244; Duplaa, C. et al. (1993) Anal. Biochem. 212:229-236.) The speed of quantitation of multiple samples may be accelerated by running the assay in a high-throughput format where the oligomer or polynucleotide of interest is presented in various dilutions and a spectrophotometric or colorimetric response gives rapid

quantitation.

In further embodiments, oligonucleotides or longer fragments derived from any of the polynucleotide sequences described herein may be used as elements on a microarray. The microarray can be used in transcript imaging techniques which monitor the relative expression levels of large numbers of genes simultaneously as described in Seilhamer, J.J. et al., "Comparative Gene Transcript Analysis," U.S. Patent No. 5,840,484, incorporated herein by reference. The microarray may also be used to identify genetic variants, mutations, and polymorphisms. This information may be used to determine gene function, to understand the genetic basis of a disorder, to diagnose a disorder, to monitor progression/regression of disease as a function of gene expression, and to develop and monitor the activities of therapeutic agents in the treatment of disease. In particular, this information may be used to develop a pharmacogenomic profile of a patient in order to select the most appropriate and effective treatment regimen for that patient. For example, therapeutic agents which are highly effective and display the fewest side effects may be selected for a patient based on his/her pharmacogenomic profile.

In another embodiment, antibodies specific for GBAP, or GBAP or fragments thereof may be used as elements on a microarray. The microarray may be used to monitor or measure protein-protein interactions, drug-target interactions, and gene expression profiles, as described above.

A particular embodiment relates to the use of the polynucleotides of the present invention to generate a transcript image of a tissue or cell type. A transcript image represents the global pattern of gene expression by a particular tissue or cell type. Global gene expression patterns are analyzed by quantifying the number of expressed genes and their relative abundance under given conditions and at a given time. (See Seilhamer et al., "Comparative Gene Transcript Analysis," U.S. Patent Number 5,840,484, expressly incorporated by reference herein.) Thus a transcript image may be generated by hybridizing the polynucleotides of the present invention or their complements to the totality of transcripts or reverse transcripts of a particular tissue or cell type. In one embodiment, the hybridization takes place in high-throughput format, wherein the polynucleotides of the present invention or their complements comprise a subset of a plurality of elements on a microarray. The resultant transcript image would provide a profile of gene activity.

Transcript images may be generated using transcripts isolated from tissues, cell lines, biopsies, or other biological samples. The transcript image may thus reflect gene expression in vivo, as in the 30 case of a tissue or biopsy sample, or in vitro, as in the case of a cell line.

Transcript images which profile the expression of the polynucleotides of the present invention may also be used in conjunction with <u>in vitro</u> model systems and preclinical evaluation of pharmaceuticals, as well as toxicological testing of industrial and naturally-occurring environmental compounds. All compounds induce characteristic gene expression patterns, frequently termed molecular fingerprints or toxicant signatures, which are indicative of mechanisms of action and toxicity

(Nuwaysir, E.F. et al. (1999) Mol. Carcinog. 24:153-159; Steiner, S. and N.L. Anderson (2000)

Toxicol. Lett. 112-113:467-471, expressly incorporated by reference herein). If a test compound has a signature similar to that of a compound with known toxicity, it is likely to share those toxic properties. These fingerprints or signatures are most useful and refined when they contain expression information from a large number of genes and gene families. Ideally, a genome-wide measurement of expression provides the highest quality signature. Even genes whose expression is not altered by any tested compounds are important as well, as the levels of expression of these genes are used to normalize the rest of the expression data. The normalization procedure is useful for comparison of expression data after treatment with different compounds. While the assignment of gene function to elements of a toxicant signature aids in interpretation of toxicity mechanisms, knowledge of gene function is not necessary for the statistical matching of signatures which leads to prediction of toxicity. (See, for example, Press Release 00-02 from the National Institute of Environmental Health Sciences, released February 29, 2000, available at http://www.niehs.nih.gov/oc/news/toxchip.htm.) Therefore, it is important and desirable in toxicological screening using toxicant signatures to include all expressed gene sequences.

In one embodiment, the toxicity of a test compound is assessed by treating a biological sample containing nucleic acids with the test compound. Nucleic acids that are expressed in the treated biological sample are hybridized with one or more probes specific to the polynucleotides of the present invention, so that transcript levels corresponding to the polynucleotides of the present invention may be quantified. The transcript levels in the treated biological sample are compared with levels in an untreated biological sample. Differences in the transcript levels between the two samples are indicative of a toxic response caused by the test compound in the treated sample.

Another particular embodiment relates to the use of the polypeptide sequences of the present invention to analyze the proteome of a tissue or cell type. The term proteome refers to the global pattern of protein expression in a particular tissue or cell type. Each protein component of a proteome can be subjected individually to further analysis. Proteome expression patterns, or profiles, are analyzed by quantifying the number of expressed proteins and their relative abundance under given conditions and at a given time. A profile of a cell's proteome may thus be generated by separating and analyzing the polypeptides of a particular tissue or cell type. In one embodiment, the separation is achieved using two-dimensional gel electrophoresis, in which proteins from a sample are separated by isoelectric focusing in the first dimension, and then according to molecular weight by sodium dodecyl sulfate slab gel electrophoresis in the second dimension (Steiner and Anderson, supra). The proteins are visualized in the gel as discrete and uniquely positioned spots, typically by staining the gel with an agent such as Coomassie Blue or silver or fluorescent stains. The optical density of each protein spot is generally proportional to the level of the protein in the sample. The optical densities of equivalently

positioned protein spots from different samples, for example, from biological samples either treated or untreated with a test compound or therapeutic agent, are compared to identify any changes in protein spot density related to the treatment. The proteins in the spots are partially sequenced using, for example, standard methods employing chemical or enzymatic cleavage followed by mass spectrometry. 5 The identity of the protein in a spot may be determined by comparing its partial sequence, preferably of at least 5 contiguous amino acid residues, to the polypeptide sequences of the present invention. In some cases, further sequence data may be obtained for definitive protein identification.

A proteomic profile may also be generated using antibodies specific for GBAP to quantify the levels of GBAP expression. In one embodiment, the antibodies are used as elements on a microarray, 10 and protein expression levels are quantified by exposing the microarray to the sample and detecting the levels of protein bound to each array element (Lueking, A. et al. (1999) Anal. Biochem. 270:103-111; Mendoze, L.G. et al. (1999) Biotechniques 27:778-788). Detection may be performed by a variety of methods known in the art, for example, by reacting the proteins in the sample with a thiol- or aminoreactive fluorescent compound and detecting the amount of fluorescence bound at each array element.

Toxicant signatures at the proteome level are also useful for toxicological screening, and should be analyzed in parallel with toxicant signatures at the transcript level. There is a poor correlation between transcript and protein abundances for some proteins in some tissues (Anderson, N.L. and J. Seilhamer (1997) Electrophoresis 18:533-537), so proteome toxicant signatures may be useful in the analysis of compounds which do not significantly affect the transcript image, but which alter the 20 proteomic profile. In addition, the analysis of transcripts in body fluids is difficult, due to rapid degradation of mRNA, so proteomic profiling may be more reliable and informative in such cases.

15

35

In another embodiment, the toxicity of a test compound is assessed by treating a biological sample containing proteins with the test compound. Proteins that are expressed in the treated biological sample are separated so that the amount of each protein can be quantified. The amount of each protein 25 is compared to the amount of the corresponding protein in an untreated biological sample. A difference in the amount of protein between the two samples is indicative of a toxic response to the test compound in the treated sample. Individual proteins are identified by sequencing the amino acid residues of the individual proteins and comparing these partial sequences to the polypeptides of the present invention.

In another embodiment, the toxicity of a test compound is assessed by treating a biological 30 sample containing proteins with the test compound. Proteins from the biological sample are incubated with antibodies specific to the polypeptides of the present invention. The amount of protein recognized by the antibodies is quantified. The amount of protein in the treated biological sample is compared with the amount in an untreated biological sample. A difference in the amount of protein between the two samples is indicative of a toxic response to the test compound in the treated sample.

Microarrays may be prepared, used, and analyzed using methods known in the art. (See, e.g.,

Brennan, T.M. et al. (1995) U.S. Patent No. 5,474,796; Schena, M. et al. (1996) Proc. Natl. Acad. Sci. USA 93:10614-10619; Baldeschweiler et al. (1995) PCT application WO95/251116; Shalon, D. et al. (1995) PCT application WO95/35505; Heller, R.A. et al. (1997) Proc. Natl. Acad. Sci. USA 94:2150-2155; and Heller, M.J. et al. (1997) U.S. Patent No. 5,605,662.) Various types of microarrays are well known and thoroughly described in DNA Microarrays: A Practical Approach, M. Schena, ed. (1999) Oxford University Press, London, hereby expressly incorporated by reference.

In another embodiment of the invention, nucleic acid sequences encoding GBAP may be used to generate hybridization probes useful in mapping the naturally occurring genomic sequence. Either coding or noncoding sequences may be used, and in some instances, noncoding sequences may be preferable over coding sequences. For example, conservation of a coding sequence among members of a multi-gene family may potentially cause undesired cross hybridization during chromosomal mapping. The sequences may be mapped to a particular chromosome, to a specific region of a chromosome, or to artificial chromosome constructions, e.g., human artificial chromosomes (HACs), yeast artificial chromosomes (YACs), bacterial artificial chromosomes (BACs), bacterial P1 constructions, or single chromosome cDNA libraries. (See, e.g., Harrington, J.J. et al. (1997) Nat. Genet. 15:345-355; Price, C.M. (1993) Blood Rev. 7:127-134; and Trask, B.J. (1991) Trends Genet. 7:149-154.) Once mapped, the nucleic acid sequences of the invention may be used to develop genetic linkage maps, for example, which correlate the inheritance of a disease state with the inheritance of a particular chromosome region or restriction fragment length polymorphism (RFLP). (See, e.g.,

Fluorescent in situ hybridization (FISH) may be correlated with other physical and genetic map data. (See, e.g., Heinz-Ulrich, et al. (1995) in Meyers, supra, pp. 965-968.) Examples of genetic map data can be found in various scientific journals or at the Online Mendelian Inheritance in Man (OMIM) World Wide Web site. Correlation between the location of the gene encoding GBAP on a physical map and a specific disorder, or a predisposition to a specific disorder, may help define the region of DNA associated with that disorder and thus may further positional cloning efforts.

In situ hybridization of chromosomal preparations and physical mapping techniques, such as linkage analysis using established chromosomal markers, may be used for extending genetic maps.

Often the placement of a gene on the chromosome of another mammalian species, such as mouse, may reveal associated markers even if the exact chromosomal locus is not known. This information is valuable to investigators searching for disease genes using positional cloning or other gene discovery techniques. Once the gene or genes responsible for a disease or syndrome have been crudely localized by genetic linkage to a particular genomic region, e.g., ataxia-telangiectasia to 11q22-23, any sequences mapping to that area may represent associated or regulatory genes for further investigation. (See, e.g., 35 Gatti, R.A. et al. (1988) Nature 336:577-580.) The nucleotide sequence of the instant invention may

also be used to detect differences in the chromosomal location due to translocation, inversion, etc., among normal, carrier, or affected individuals.

In another embodiment of the invention, GBAP, its catalytic or immunogenic fragments, or oligopeptides thereof can be used for screening libraries of compounds in any of a variety of drug screening techniques. The fragment employed in such screening may be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. The formation of binding complexes between GBAP and the agent being tested may be measured.

Another technique for drug screening provides for high throughput screening of compounds having suitable binding affinity to the protein of interest. (See, e.g., Geysen, et al. (1984) PCT application WO84/03564.) In this method, large numbers of different small test compounds are synthesized on a solid substrate. The test compounds are reacted with GBAP, or fragments thereof, and washed. Bound GBAP is then detected by methods well known in the art. Purified GBAP can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

In another embodiment, one may use competitive drug screening assays in which neutralizing antibodies capable of binding GBAP specifically compete with a test compound for binding GBAP. In this manner, antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with GBAP.

In additional embodiments, the nucleotide sequences which encode GBAP may be used in any molecular biology techniques that have yet to be developed, provided the new techniques rely on properties of nucleotide sequences that are currently known, including, but not limited to, such properties as the triplet genetic code and specific base pair interactions.

Without further claboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

The disclosures of all patents, applications and publications, mentioned above and below, in particular U.S. Ser. No. 60/144,595, U.S Ser. No. 60/150,460, and U.S. Ser. No. 60/159,849, are hereby expressly incorporated by reference.

30

15

EXAMPLES

I. Construction of cDNA Libraries

RNA was purchased from Clontech or isolated from tissues described in Table 4. Some tissues were homogenized and lysed in guanidinium isothiocyanate, while others were homogenized and lysed in phenol or in a suitable mixture of denaturants, such as TRIZOL (Life Technologies), a monophasic

solution of phenol and guanidine isothiocyanate. The resulting lysates were centrifuged over CsCl cushions or extracted with chloroform. RNA was precipitated from the lysates with either isopropanol or sodium acetate and ethanol, or by other routine methods.

Phenol extraction and precipitation of RNA were repeated as necessary to increase RNA

5 purity. In some cases, RNA was treated with DNase. For most libraries, poly(A+) RNA was isolated using oligo d(T)-coupled paramagnetic particles (Promega), OLIGOTEX latex particles (QIAGEN, Chatsworth CA), or an OLIGOTEX mRNA purification kit (QIAGEN). Alternatively, RNA was isolated directly from tissue lysates using other RNA isolation kits, e.g., the POLY(A)PURE mRNA purification kit (Ambion, Austin TX).

- In some cases, Stratagene was provided with RNA and constructed the corresponding cDNA libraries. Otherwise, cDNA was synthesized and cDNA libraries were constructed with the UNIZAP vector system (Stratagene) or SUPERSCRIPT plasmid system (Life Technologies), using the recommended procedures or similar methods known in the art. (See, e.g., Ausubel, 1997, supra, units 5.1-6.6.) Reverse transcription was initiated using oligo d(T) or random primers. Synthetic
- oligonucleotide adapters were ligated to double stranded cDNA, and the cDNA was digested with the appropriate restriction enzyme or enzymes. For most libraries, the cDNA was size-selected (300-1000 bp) using SEPHACRYL S1000, SEPHAROSE CL2B, or SEPHAROSE CL4B column chromatography (Amersham Pharmacia Biotech) or preparative agarose gel electrophoresis. cDNAs were ligated into compatible restriction enzyme sites of the polylinker of a suitable plasmid, e.g.,
- 20 PBLUESCRIPT plasmid (Stratagene), PSPORT1 plasmid (Life Technologies), pcDNA2.1 plasmid (Invitrogen, Carlsbad CA), or pINCY plasmid (Incyte Genomics, Palo Alto CA). Recombinant plasmids were transformed into competent <u>E. coli</u> cells including XL1-Blue, XL1-BlueMRF, or SOLR from Stratagene or DH5α, DH10B, or ElectroMAX DH10B from Life Technologies.

II. Isolation of cDNA Clones

Plasmids obtained as described in Example I were recovered from host cells by in vivo excision using the UNIZAP vector system (Stratagene) or by cell lysis. Plasmids were purified using at least one of the following: a Magic or WIZARD Minipreps DNA purification system (Promega); an AGTC Miniprep purification kit (Edge Biosystems, Gaithersburg MD); and QIAWELL 8 Plasmid, QIAWELL 8 Plasmid, QIAWELL 8 Ultra Plasmid purification systems or the R.E.A.L. PREP 96 plasmid purification kit from QIAGEN. Following precipitation, plasmids were resuspended in 0.1 ml of distilled water and stored, with or without lyophilization, at 4°C.

Alternatively, plasmid DNA was amplified from host cell lysates using direct link PCR in a high-throughput format (Rao, V.B. (1994) Anal. Biochem. 216:1-14). Host cell lysis and thermal cycling steps were carried out in a single reaction mixture. Samples were processed and stored in 384-35 well plates, and the concentration of amplified plasmid DNA was quantified fluorometrically using

PICOGREEN dye (Molecular Probes, Eugene OR) and a FLUOROSKAN II fluorescence scanner (Labsystems Oy, Helsinki, Finland).

III. Sequencing and Analysis

Incyte cDNA recovered in plasmids as described in Example II were sequenced as follows.

- 5 Sequencing reactions were processed using standard methods or high-throughput instrumentation such as the ABI CATALYST 800 (PE Biosystems) thermal cycler or the PTC-200 thermal cycler (MJ Research) in conjunction with the HYDRA microdispenser (Robbins Scientific) or the MICROLAB 2200 (Hamilton) liquid transfer system. cDNA sequencing reactions were prepared using reagents provided by Amersham Pharmacia Biotech or supplied in ABI sequencing kits such as the ABI
- PRISM BIGDYE Terminator cycle sequencing ready reaction kit (PE Biosystems). Electrophoretic separation of cDNA sequencing reactions and detection of labeled polynucleotides were carried out using the MEGABACE 1000 DNA sequencing system (Molecular Dynamics); the ABI PRISM 373 or 377 sequencing system (PE Biosystems) in conjunction with standard ABI protocols and base calling software; or other sequence analysis systems known in the art. Reading frames within the cDNA
 15 sequences were identified using standard methods (reviewed in Ausubel, 1997, supra unit 7.7). Some

15 sequences were identified using standard methods (reviewed in Ausubel, 1997, <u>supra</u>, unit 7.7). Some of the cDNA sequences were selected for extension using the techniques disclosed in Example VI.

The polynucleotide sequences derived from cDNA sequencing were assembled and analyzed using a combination of software programs which utilize algorithms well known to those skilled in the art. Table 5 summarizes the tools, programs, and algorithms used and provides applicable descriptions, references, and threshold parameters. The first column of Table 5 shows the tools, programs, and algorithms used, the second column provides brief descriptions thereof, the third column presents appropriate references, all of which are incorporated by reference herein in their entirety, and the fourth column presents, where applicable, the scores, probability values, and other parameters used to evaluate the strength of a match between two sequences (the higher the score, the greater the homology between two sequences). Sequences were analyzed using MACDNASIS PRO software (Hitachi Software Engineering, South San Francisco CA) and LASERGENE software (DNASTAR). Polynucleotide and polypeptide sequence alignments were generated using the default parameters specified by the clustal algorithm as incorporated into the MEGALIGN multisequence alignment program (DNASTAR), which

The polynucleotide sequences were validated by removing vector, linker, and polyA sequences and by masking ambiguous bases, using algorithms and programs based on BLAST, dynamic programing, and dinucleotide nearest neighbor analysis. The sequences were then queried against a selection of public databases such as the GenBank primate, rodent, mammalian, vertebrate, and eukaryote databases, and BLOCKS, PRINTS, DOMO, PRODOM, and PFAM to acquire annotation using programs based on BLAST, FASTA, and BLIMPS. The sequences were assembled into full

also calculates the percent identity between aligned sequences.

length polynucleotide sequences using programs based on Phred, Phrap, and Consed, and were screened for open reading frames using programs based on GeneMark, BLAST, and FASTA. The full length polynucleotide sequences were translated to derive the corresponding full length amino acid sequences, and these full length sequences were subsequently analyzed by querying against databases such as the GenBank databases (described above), SwissProt, BLOCKS, PRINTS, DOMO, PRODOM, Prosite, and Hidden Markov Model (HMM)-based protein family databases such as PFAM. HMM is a probabilistic approach which analyzes consensus primary structures of gene families. (See, e.g., Eddy, S.R. (1996) Curr. Opin. Struct. Biol. 6:361-365.)

The programs described above for the assembly and analysis of full length polynucleotide and amino acid sequences were also used to identify polynucleotide sequence fragments from SEQ ID NO:67-132. Fragments from about 20 to about 4000 nucleotides which are useful in hybridization and amplification technologies were described in The Invention section above.

IV. Analysis of Polynucleotide Expression

Northern analysis is a laboratory technique used to detect the presence of a transcript of a gene and involves the hybridization of a labeled nucleotide sequence to a membrane on which RNAs from a particular cell type or tissue have been bound. (See, e.g., Sambrook, supra, ch. 7; Ausubel, 1995, supra, ch. 4 and 16.)

Analogous computer techniques applying BLAST were used to search for identical or related molecules in cDNA databases such as GenBank or LIFESEQ (Incyte Genomics). This analysis is much faster than multiple membrane-based hybridizations. In addition, the sensitivity of the computer search can be modified to determine whether any particular match is categorized as exact or similar. The basis of the search is the product score, which is defined as:

BLAST Score x Percent Identity

5 x minimum {length(Seq. 1), length(Seq. 2)}

25

The product score takes into account both the degree of similarity between two sequences and the length of the sequence match. The product score is a normalized value between 0 and 100, and is calculated as follows: the BLAST score is multiplied by the percent nucleotide identity and the product is divided by (5 times the length of the shorter of the two sequences). The BLAST score is calculated by assigning a score of +5 for every base that matches in a high-scoring segment pair (HSP), and -4 for every mismatch. Two sequences may share more than one HSP (separated by gaps). If there is more than one HSP, then the pair with the highest BLAST score is used to calculate the product score. The product score represents a balance between fractional overlap and quality in a BLAST alignment. For example, a product score of 100 is produced only for 100% identity over the entire length of the shorter of the two sequences being compared. A product score of 70 is produced either by 100% identity and

70% overlap at one end, or by 88% identity and 100% overlap at the other. A product score of 50 is produced either by 100% identity and 50% overlap at one end, or 79% identity and 100% overlap.

The results of northern analyses are reported as a percentage distribution of libraries in which the transcript encoding GBAP occurred. Analysis involved the categorization of cDNA libraries by organ/tissue and disease. The organ/tissue categories included cardiovascular, dermatologic, developmental, endocrine, gastrointestinal, hematopoietic/immune, musculoskeletal, nervous, reproductive, and urologic. The disease/condition categories included cancer, inflammation, trauma, cell proliferation, neurological, and pooled. For each category, the number of libraries expressing the sequence of interest was counted and divided by the total number of libraries across all categories.

10 Percentage values of tissue-specific and disease- or condition-specific expression are reported in Table3.

V. Chromosomal Mapping of GBAP Encoding Polynucleotides

The cDNA sequences which were used to assemble SEQ ID NO:67-132 were compared with sequences from the Incyte LIFESEQ database and public domain databases using BLAST and other implementations of the Smith-Waterman algorithm. Sequences from these databases that matched SEQ ID NO:67-132 were assembled into clusters of contiguous and overlapping sequences using assembly algorithms such as Phrap (Table 5). Radiation hybrid and genetic mapping data available from public resources such as the Stanford Human Genome Center (SHGC), Whitehead Institute for Genome Research (WIGR), and Généthon were used to determine if any of the clustered sequences had been previously mapped. Inclusion of a mapped sequence in a cluster resulted in the assignment of all sequences of that cluster, including its particular SEQ ID NO:, to that map location.

The genetic máp locations of SEQ ID NO:70, 74, 75, 77, 80, 86, 87, 90, 92, 93, 94, 97, 101, 106, 109, 111, 112, 113, 115, 117, 118, 121, and 128 are described in The Invention as ranges, or intervals, of human chromosomes. More than one map location is reported for SEQ ID NO:94, 101, 109, 111, and 115, indicating that previously mapped sequences having similarity, but not complete identity, to SEQ ID NO:94, 101, 109, 111, and 115 were assembled into their respective clusters. The map position of an interval, in centiMorgans, is measured relative to the terminus of the chromosome's p-arm. (The centiMorgan (cM) is a unit of measurement based on recombination frequencies between chromosomal markers. On average, 1 cM is roughly equivalent to 1 megabase (Mb) of DNA in humans, although this can vary widely due to hot and cold spots of recombination.) The cM distances are based on genetic markers mapped by Généthon which provide boundaries for radiation hybrid markers whose sequences were included in each of the clusters.

VI. Extension of GBAP Encoding Polynucleotides

The full length nucleic acid sequences of SEQ ID NO:67-132 were produced by extension of an appropriate fragment of the full length molecule using oligonucleotide primers designed from this

fragment. One primer was synthesized to initiate 5' extension of the known fragment, and the other primer, to initiate 3' extension of the known fragment. The initial primers were designed using OLIGO 4.06 software (National Biosciences), or another appropriate program, to be about 22 to 30 nucleotides in length, to have a GC content of about 50% or more, and to anneal to the target sequence at temperatures of about 68°C to about 72°C. Any stretch of nucleotides which would result in hairpin structures and primer-primer dimerizations was avoided.

Selected human cDNA libraries were used to extend the sequence. If more than one extension was necessary or desired, additional or nested sets of primers were designed.

High fidelity amplification was obtained by PCR using methods well known in the art. PCR was performed in 96-well plates using the PTC-200 thermal cycler (MJ Research, Inc.). The reaction mix contained DNA template, 200 nmol of each primer, reaction buffer containing Mg²⁺, (NH₄)₂SO₄, and β-mercaptoethanol, Taq DNA polymerase (Amersham Pharmacia Biotech), ELONGASE enzyme (Life Technologies), and Pfu DNA polymerase (Stratagene), with the following parameters for primer pair PCI A and PCI B: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C. In the alternative, the parameters for primer pair T7 and SK+ were as follows: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 57°C, 1 min; Step 4: 68°C, 2 min; Step 5: Steps 2, 3, and 4 repeated 20 times; Step 6: 68°C, 5 min; Step 7: storage at 4°C.

The concentration of DNA in each well was determined by dispensing 100 μ l PICOGREEN quantitation reagent (0.25% (v/v) PICOGREEN; Molecular Probes, Eugene OR) dissolved in 1X TE and 0.5 μ l of undiluted PCR product into each well of an opaque fluorimeter plate (Corning Costar, Acton MA), allowing the DNA to bind to the reagent. The plate was scanned in a Fluoroskan II (Labsystems Oy, Helsinki, Finland) to measure the fluorescence of the sample and to quantify the concentration of DNA. A 5 μ l to 10 μ l aliquot of the reaction mixture was analyzed by electrophoresis on a 1% agarose mini-gel to determine which reactions were successful in extending the sequence.

The extended nucleotides were desalted and concentrated, transferred to 384-well plates, digested with CviJI cholera virus endonuclease (Molecular Biology Research, Madison WI), and sonicated or sheared prior to religation into pUC 18 vector (Amersham Pharmacia Biotech). For shotgun sequencing, the digested nucleotides were separated on low concentration (0.6 to 0.8%) agarose gels, fragments were excised, and agar digested with Agar ACE (Promega). Extended clones were religated using T4 ligase (New England Biolabs, Beverly MA) into pUC 18 vector (Amersham Pharmacia Biotech), treated with Pfu DNA polymerase (Stratagene) to fill-in restriction site overhangs, and transfected into competent <u>E. coli</u> cells. Transformed cells were selected on antibiotic-containing media, and individual colonies were picked and cultured overnight at 37°C in 384-well plates in LB/2x carb liquid media.

The cells were lysed, and DNA was amplified by PCR using Taq DNA polymerase (Amersham Pharmacia Biotech) and Pfu DNA polymerase (Stratagene) with the following parameters: Step 1: 94°C, 3 min; Step 2: 94°C, 15 sec; Step 3: 60°C, 1 min; Step 4: 72°C, 2 min; Step 5: steps 2, 3, and 4 repeated 29 times; Step 6: 72°C, 5 min; Step 7: storage at 4°C. DNA was quantified by PICOGREEN reagent (Molecular Probes) as described above. Samples with low DNA recoveries were reamplified using the same conditions as described above. Samples were diluted with 20% dimethysulfoxide (1:2, v/v), and sequenced using DYENAMIC energy transfer sequencing primers and the DYENAMIC DIRECT kit (Amersham Pharmacia Biotech) or the ABI PRISM BIGDYE Terminator cycle sequencing ready reaction kit (PE Biosystems).

In like manner, the polynucleotide sequences of SEQ ID NO:67-132 are used to obtain 5' regulatory sequences using the procedure above, along with oligonucleotides designed for such extension, and an appropriate genomic library.

VII. Labeling and Use of Individual Hybridization Probes

Hybridization probes derived from SEQ ID NO:67-132 are employed to screen cDNAs, genomic DNAs, or mRNAs. Although the labeling of oligonucleotides, consisting of about 20 base pairs, is specifically described, essentially the same procedure is used with larger nucleotide fragments. Oligonucleotides are designed using state-of-the-art software such as OLIGO 4.06 software (National Biosciences) and labeled by combining 50 pmol of each oligomer, 250 μCi of [γ-³²P] adenosine triphosphate (Amersham Pharmacia Biotech), and T4 polynucleotide kinase (DuPont NEN, Boston MA). The labeled oligonucleotides are substantially purified using a SEPHADEX G-25 superfine size exclusion dextran bead column (Amersham Pharmacia Biotech). An aliquot containing 10⁷ counts per minute of the labeled probe is used in a typical membrane-based hybridization analysis of human genomic DNA digested with one of the following endonucleases: Ase I, Bgl II, Eco RI, Pst I, Xba I, or Pvu II (DuPont NEN).

The DNA from each digest is fractionated on a 0.7% agarose gel and transferred to nylon membranes (Nytran Plus, Schleicher & Schuell, Durham NH). Hybridization is carried out for 16 hours at 40°C. To remove nonspecific signals, blots are sequentially washed at room temperature under conditions of up to, for example, 0.1 x saline sodium citrate and 0.5% sodium dodecyl sulfate. Hybridization patterns are visualized using autoradiography or an alternative imaging means and compared.

VIII. Microarrays

The linkage or synthesis of array elements upon a microarray can be achieved utilizing photolithography, piezoelectric printing (ink-jet printing, See, e.g., Baldeschweiler, supra), mechanical microspotting technologies, and derivatives thereof. The substrate in each of the aforementioned technologies should be uniform and solid with a non-porous surface (Schena (1999), supra). Suggested

substrates include silicon, silica, glass slides, glass chips, and silicon wafers. Alternatively, a procedure analogous to a dot or slot blot may also be used to arrange and link elements to the surface of a substrate using thermal, UV, chemical, or mechanical bonding procedures. A typical array may be produced using available methods and machines well known to those of ordinary skill in the art and may contain any appropriate number of elements. (Scc, c.g., Schena, M. et al. (1995) Science 270:467-470; Shalon, D. et al. (1996) Genome Res. 6:639-645; Marshall, A. and J. Hodgson (1998) Nat. Biotechnol. 16:27-31.)

Full length cDNAs, Expressed Sequence Tags (ESTs), or fragments or oligomers thereof may comprise the elements of the microarray. Fragments or oligomers suitable for hybridization can be selected using software well known in the art such as LASERGENE software (DNASTAR). The array elements are hybridized with polynucleotides in a biological sample. The polynucleotides in the biological sample are conjugated to a fluorescent label or other molecular tag for ease of detection. After hybridization, nonhybridized nucleotides from the biological sample are removed, and a fluorescence scanner is used to detect hybridization at each array element. Alternatively, laser desorbtion and mass spectrometry may be used for detection of hybridization. The degree of complementarity and the relative abundance of each polynucleotide which hybridizes to an element on the microarray may be assessed. In one embodiment, microarray preparation and usage is described in detail below.

Tissue or Cell Sample Preparation

Total RNA is isolated from tissue samples using the guanidinium thiocyanate method and 20 poly(A)* RNA is purified using the oligo-(dT) cellulose method. Each poly(A)* RNA sample is reverse transcribed using MMLV reverse-transcriptase, 0.05 pg/µl oligo-(dT) primer (21mer), 1X first strand buffer, 0.03 units/µl RNase inhibitor, 500 µM dATP, 500 µM dGTP, 500 µM dTTP, 40 µM dCTP, 40 µM dCTP-Cy3 (BDS) or dCTP-Cy5 (Amersham Pharmacia Biotech). The reverse 25 transcription reaction is performed in a 25 ml volume containing 200 ng poly(A)⁺ RNA with GEMBRIGHT kits (Incyte). Specific control poly(A)* RNAs are synthesized by in vitro transcription from non-coding yeast genomic DNA. After incubation at 37 °C for 2 hr, each reaction sample (one with Cy3 and another with Cy5 labeling) is treated with 2.5 ml of 0.5M sodium hydroxide and incubated for 20 minutes at 85 °C to the stop the reaction and degrade the RNA. Samples are purified 30 using two successive CHROMA SPIN 30 gel filtration spin columns (CLONTECH Laboratories, Inc. (CLONTECH), Palo Alto CA) and after combining, both reaction samples are ethanol precipitated using 1 ml of glycogen (1 mg/ml), 60 ml sodium acetate, and 300 ml of 100% ethanol. The sample is then dried to completion using a SpeedVAC (Savant Instruments Inc., Holbrook NY) and resuspended in 14 µl 5X SSC/0.2% SDS.

35 Microarray Preparation

Sequences of the present invention are used to generate array elements. Each array element is amplified from bacterial cells containing vectors with cloned cDNA inserts. PCR amplification uses primers complementary to the vector sequences flanking the cDNA insert. Array elements are amplified in thirty cycles of PCR from an initial quantity of 1-2 ng to a final quantity greater than 5 pg. Amplified array elements are then purified using SEPHACRYL-400 (Amersham Pharmacia Biotech).

Purified array elements are immobilized on polymer-coated glass slides. Glass microscope slides (Corning) are cleaned by ultrasound in 0.1% SDS and acetone, with extensive distilled water washes between and after treatments. Glass slides are etched in 4% hydrofluoric acid (VWR 10 Scientific Products Corporation (VWR), West Chester PA), washed extensively in distilled water, and coated with 0.05% aminopropyl silane (Sigma) in 95% ethanol. Coated slides are cured in a 110°C oven.

Array elements are applied to the coated glass substrate using a procedure described in US Patent No. 5,807,522, incorporated herein by reference. 1 µl of the array element DNA, at an average concentration of 100 ng/µl, is loaded into the open capillary printing element by a high-speed robotic apparatus. The apparatus then deposits about 5 nl of array element sample per slide.

Microarrays are UV-crosslinked using a STRATALINKER UV-crosslinker (Stratagene). Microarrays are washed at room temperature once in 0.2% SDS and three times in distilled water. Non-specific binding sites are blocked by incubation of microarrays in 0.2% casein in phosphate buffered saline (PBS) (Tropix, Inc., Bedford MA) for 30 minutes at 60 °C followed by washes in 0.2% SDS and distilled water as before.

Hybridization

Hybridization reactions contain 9 μl of sample mixture consisting of 0.2 μg each of Cy3 and Cy5 labeled cDNA synthesis products in 5X SSC, 0.2% SDS hybridization buffer. The sample mixture is heated to 65 °C for 5 minutes and is aliquoted onto the microarray surface and covered with an 1.8 cm² coverslip. The arrays are transferred to a waterproof chamber having a cavity just slightly larger than a microscope slide. The chamber is kept at 100% humidity internally by the addition of 140 μl of 5X SSC in a corner of the chamber. The chamber containing the arrays is incubated for about 6.5 hours at 60 °C. The arrays are washed for 10 min at 45 °C in a first wash buffer (1X SSC, 0.1% SDS), three times for 10 minutes each at 45 °C in a second wash buffer (0.1X SSC), and dried.

Reporter-labeled hybridization complexes are detected with a microscope equipped with an Innova 70 mixed gas 10 W laser (Coherent, Inc., Santa Clara CA) capable of generating spectral lines at 488 nm for excitation of Cy3 and at 632 nm for excitation of Cy5. The excitation laser light is focused on the array using a 20X microscope objective (Nikon, Inc., Melville NY). The slide

containing the array is placed on a computer-controlled X-Y stage on the microscope and raster-scanned past the objective. The 1.8 cm x 1.8 cm array used in the present example is scanned with a resolution of 20 micrometers.

In two separate scans, a mixed gas multiline laser excites the two fluorophores sequentially.

5 Emitted light is split, based on wavelength, into two photomultiplier tube detectors (PMT R1477, Hamamatsu Photonics Systems, Bridgewater NJ) corresponding to the two fluorophores. Appropriate filters positioned between the array and the photomultiplier tubes are used to filter the signals. The emission maxima of the fluorophores used are 565 nm for Cy3 and 650 nm for Cy5. Each array is typically scanned twice, one scan per fluorophore using the appropriate filters at the laser source, although the apparatus is capable of recording the spectra from both fluorophores simultaneously.

The sensitivity of the scans is typically calibrated using the signal intensity generated by a cDNA control species added to the sample mixture at a known concentration. A specific location on the array contains a complementary DNA sequence, allowing the intensity of the signal at that location to be correlated with a weight ratio of hybridizing species of 1:100,000. When two samples from different sources (e.g., representing test and control cells), each labeled with a different fluorophore, are hybridized to a single array for the purpose of identifying genes that are differentially expressed, the calibration is done by labeling samples of the calibrating cDNA with the two fluorophores and adding identical amounts of each to the hybridization mixture.

The output of the photomultiplier tube is digitized using a 12-bit RTI-835H analog-to-digital (A/D) conversion board (Analog Devices, Inc., Norwood MA) installed in an IBM-compatible PC computer. The digitized data are displayed as an image where the signal intensity is mapped using a linear 20-color transformation to a pseudocolor scale ranging from blue (low signal) to red (high signal). The data is also analyzed quantitatively. Where two different fluorophores are excited and measured simultaneously, the data are first corrected for optical crosstalk (due to overlapping emission spectra) between the fluorophores using each fluorophore's emission spectrum.

A grid is superimposed over the fluorescence signal image such that the signal from each spot is centered in each element of the grid. The fluorescence signal within each element is then integrated to obtain a numerical value corresponding to the average intensity of the signal. The software used for signal analysis is the GEMTOOLS gene expression analysis program (Incyte).

30 IX. Complementary Polynucleotides

Sequences complementary to the GBAP-encoding sequences, or any parts thereof, are used to detect, decrease, or inhibit expression of naturally occurring GBAP. Although use of oligonucleotides comprising from about 15 to 30 base pairs is described, essentially the same procedure is used with smaller or with larger sequence fragments. Appropriate oligonucleotides are designed using OLIGO 4.06 software (National Biosciences) and the coding sequence of GBAP. To inhibit transcription, a

complementary oligonucleotide is designed from the most unique 5' sequence and used to prevent promoter binding to the coding sequence. To inhibit translation, a complementary oligonucleotide is designed to prevent ribosomal binding to the GBAP-encoding transcript.

X. Expression of GBAP

5 Expression and purification of GBAP is achieved using bacterial or virus-based expression systems. For expression of GBAP in bacteria, cDNA is subcloned into an appropriate vector containing an antibiotic resistance gene and an inducible promoter that directs high levels of cDNA transcription. Examples of such promoters include, but are not limited to, the trp-lac (tac) hybrid promoter and the T5 or T7 bacteriophage promoter in conjunction with the lac operator regulatory 10 element. Recombinant vectors are transformed into suitable bacterial hosts, e.g., BL21(DE3). Antibiotic resistant bacteria express GBAP upon induction with isopropyl beta-Dthiogalactopyranoside (IPTG). Expression of GBAP in eukaryotic cells is achieved by infecting insect or mammalian cell lines with recombinant Autographica californica nuclear polyhedrosis virus (AcMNPV), commonly known as baculovirus. The nonessential polyhedrin gene of baculovirus is 15 replaced with cDNA encoding GBAP by either homologous recombination or bacterial-mediated transposition involving transfer plasmid intermediates. Viral infectivity is maintained and the strong polyhedrin promoter drives high levels of cDNA transcription. Recombinant baculovirus is used to infect Spodoptera frugiperda (Sf9) insect cells in most cases, or human hepatocytes, in some cases. Infection of the latter requires additional genetic modifications to baculovirus. (See Engelhard, E.K. et 20 al. (1994) Proc. Natl. Acad. Sci. USA 91:3224-3227; Sandig, V. et al. (1996) Hum. Gene Ther. 7:1937-1945.)

In most expression systems, GBAP is synthesized as a fusion protein with, e.g., glutathione Stransferase (GST) or a peptide epitope tag, such as FLAG or 6-His, permitting rapid, single-step, affinity-based purification of recombinant fusion protein from crude cell lysates. GST, a 26-kilodalton enzyme from Schistosoma japonicum, enables the purification of fusion proteins on immobilized glutathione under conditions that maintain protein activity and antigenicity (Amersham Pharmacia Biotech). Following purification, the GST moiety can be proteolytically cleaved from GBAP at specifically engineered sites. FLAG, an 8-amino acid peptide, enables immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies (Eastman Kodak). 6-His, a stretch of six consecutive histidine residues, enables purification on metal-chelate resins (QIAGEN). Methods for protein expression and purification are discussed in Ausubel (1995, supra, ch. 10 and 16). Purified GBAP obtained by these methods can be used directly in the assays shown in

XI. Demonstration of GBAP Activity

Examples XI and XV.

35 GTP-binding activity of GBAP is determined in an assay that measures the binding of GBAP

to α-P³²-labeled GTP. Purified GBAP is first blotted onto filters and rinsed in a suitable buffer. The filters are then incubated in buffer containing radiolabeled α-³²P-GTP. The filters are washed in buffer to remove unbound GTP and counted in a radioisotope counter. Non-specific binding is determined in an assay that contains a 100-fold excess of unlabeled GTP. The amount of specific binding is proportional to the activity of GBAP.

GTPase activity of GBAP is determined in an assay that measures the conversion of α-³²P-GTP to α-³²P-GDP. GBAP is incubated with α-³²P-GTP in buffer for an appropriate period of time, and the reaction is terminated by heating or acid precipitation followed by centrifugation. An aliquot of the supernatant is subjected to polyacrylamide gel electrophoresis (PAGE) to separate GDP and GTP together with unlabeled standards. The GDP spot is cut out and counted in a radioisotope counter. The amount of radioactivity recovered in GDP is proportional to GTPase activity of GBAP.

XII. Functional Assays

GBAP function is assessed by expressing the sequences encoding GBAP at physiologically elevated levels in mammalian cell culture systems. cDNA is subcloned into a mammalian expression 15 vector containing a strong promoter that drives high levels of cDNA expression. Vectors of choice include pCMV SPORT plasmid (Life Technologies) and pCR3.1 plasmid (Invitrogen), both of which contain the cytomegalovirus promoter. 5-10 μ g of recombinant vector are transiently transfected into a human cell line, for example, an endothelial or hematopoietic cell line, using either liposome formulations or electroporation. 1-2 μ g of an additional plasmid containing sequences encoding a 20 marker protein are co-transfected. Expression of a marker protein provides a means to distinguish. transfected cells from nontransfected cells and is a reliable predictor of cDNA expression from the recombinant vector. Marker proteins of choice include, e.g., Green Fluorescent Protein (GFP; Clontech), CD64, or a CD64-GFP fusion protein. Flow cytometry (FCM), an automated, laser opticsbased technique, is used to identify transfected cells expressing GFP or CD64-GFP and to evaluate the 25 apoptotic state of the cells and other cellular properties. FCM detects and quantifies the uptake of fluorescent molecules that diagnose events preceding or coincident with cell death. These events include changes in nuclear DNA content as measured by staining of DNA with propidium iodide; changes in cell size and granularity as measured by forward light scatter and 90 degree side light scatter; downregulation of DNA synthesis as measured by decrease in bromodcoxyuridine uptake; alterations in 30 expression of cell surface and intracellular proteins as measured by reactivity with specific antibodies; and alterations in plasma membrane composition as measured by the binding of fluorescein-conjugated Annexin V protein to the cell surface. Methods in flow cytometry are discussed in Ormerod, M.G. (1994) Flow Cytometry, Oxford, New York NY.

The influence of GBAP on gene expression can be assessed using highly purified populations of cells transfected with sequences encoding GBAP and either CD64 or CD64-GFP. CD64 and CD64-

GFP are expressed on the surface of transfected cells and bind to conserved regions of human immunoglobulin G (IgG). Transfected cells are efficiently separated from nontransfected cells using magnetic beads coated with either human IgG or antibody against CD64 (DYNAL, Lake Success NY). mRNA can be purified from the cells using methods well known by those of skill in the art. Expression of mRNA encoding GBAP and other genes of interest can be analyzed by northern analysis or microarray techniques.

XIII. Production of GBAP Specific Antibodies

GBAP substantially purified using polyacrylamide gel electrophoresis (PAGE; see, e.g., Harrington, M.G. (1990) Methods Enzymol. 182:488-495), or other purification techniques, is used to immunize rabbits and to produce antibodies using standard protocols.

Alternatively, the GBAP amino acid sequence is analyzed using LASERGENE software (DNASTAR) to determine regions of high immunogenicity, and a corresponding oligopeptide is synthesized and used to raise antibodies by means known to those of skill in the art. Methods for selection of appropriate epitopes, such as those near the C-terminus or in hydrophilic regions are well described in the art. (See, e.g., Ausubel, 1995, supra, ch. 11.)

Typically, oligopeptides of about 15 residues in length are synthesized using an ABI 431A peptide synthesizer (PE Biosystems) using FMOC chemistry and coupled to KLH (Sigma-Aldrich, St. Louis MO) by reaction with N-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS) to increase immunogenicity. (See, e.g., Ausubel, 1995, supra.) Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. Resulting antisera are tested for antipeptide and anti-GBAP activity by, for example, binding the peptide or GBAP to a substrate, blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radio-iodinated goat anti-rabbit IgG.

XIV. Purification of Naturally Occurring GBAP Using Specific Antibodies

Naturally occurring or recombinant GBAP is substantially purified by immunoaffinity chromatography using antibodies specific for GBAP. An immunoaffinity column is constructed by covalently coupling anti-GBAP antibody to an activated chromatographic resin, such as CNBr-activated SEPHAROSE (Amersham Pharmacia Biotech). After the coupling, the resin is blocked and washed according to the manufacturer's instructions.

Media containing GBAP are passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of GBAP (e.g., high ionic strength buffers in the presence of detergent). The column is eluted under conditions that disrupt antibody/GBAP binding (e.g., a buffer of pH 2 to pH 3, or a high concentration of a chaotrope, such as urea or thiocyanate ion), and GBAP is collected.

XV. Identification of Molecules Which Interact with GBAP

35 GBAP, or biologically active fragments thereof, are labeled with ¹²⁵I Bolton-Hunter reagent.

(See, e.g., Bolton A.E. and W.M. Hunter (1973) Biochem. J. 133:529-539.) Candidate molecules previously arrayed in the wells of a multi-well plate are incubated with the labeled GBAP, washed, and any wells with labeled GBAP complex are assayed. Data obtained using different concentrations of GBAP are used to calculate values for the number, affinity, and association of GBAP with the 5 candidate molecules.

Alternatively, molecules interacting with GBAP are analyzed using the yeast two-hybrid system as described in Fields, S. and O. Song (1989, Nature 340:245-246), or using commercially available kits based on the two-hybrid system, such as the MATCHMAKER system (Clontech).

GBAP may also be used in the PATHCALLING process (CuraGen Corp., New Haven CT)
which employs the yeast two-hybrid system in a high-throughput manner to determine all interactions between the proteins encoded by two large libraries of genes (Nandabalan, K. et al. (2000) U.S. Patent No. 6,057,101).

Various modifications and variations of the described methods and systems of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention.

Although the invention has been described in connection with certain embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments.

Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in molecular biology or related fields are intended to be within the scope of the following claims.

Table 1

Ī													,
	Fragments	1405545F6 (LATRTUT02), 1405545H1 (LATRTUT02), 2926327F7 (TLYMNOT04), 2926327F6	700515X14 (SYNORAT03), 758541H1 (BRAITUT02), 1348685F6 (PROSNOT11), 1451265H1 (PENITUT01), 1872777F6 (LEUKNOT02)	1556311H1 (BLADTUT04), 3221281T6 (COLNNON03), 3350311F6 (BRAITUT24), SBFA02256F1, SBFA01440F1, SBFA01098F1, SBFA041F1	RAITUTO2), 1255 , 1901373H1 (BI BRSTNOT19), 321 , 4319601H1 (BE	1331124F1 (PANCNOTO7), 2367767H1 (ADRENOTO7), 2367779F6 (ADRENOTO7), 2782232F6 (BRSTNOT13), 3079286H2 (BRAIUNTO1), 3584043T6 (293TF4T01), 4994696H1 (LIVRTUT11)	312565H1 (LUNGNOTO2), 841829R6 (PROSTUTO5), 1340809H1 (COLNTUTO3), 1842057H1 (COLNNOTO7), 2693513F6 (LUNGNOT23), 3090433H1 (BRSTNOT19), 4895874H1 (LIVRTUT12)	554715F1 (SCORNOTO1), 882035X23 (THYRNOTO2), 3042234F7 (BRSTNOT16), 3630695H1 (COLNNOT38), 3800591H1 (SPLNNOT12), 4975447H1 (HELATXT03)	> 2	1001977P1 (BRSTNOT03), 1312045F1 (COLNFET02), 1334040F2 (COLNNOT13), 1488082F6 (UCMCL5T01), 1570077F1 (UTRSNOT05), 1929845H1 (COLNTUT03), 230606H1 (NGANNOT01), 3127730F7 (LUNGTUT12), 3494367H1 (ADRETUT07), 3578924H1 (293TF3T01), 4619513H1 (ENDVNOT01), 4932823H1 (BRSTTUT20), 5324322H1 (FIBPFEN06)	067184H1 (HUVESTB01), 067184R1 (HUVESTB01), 067184X12 (HUVESTB01), 067184X23C1 (HUVESTB01), 067184X29C1 (HUVESTB01), 968551H1 (BRSTNOT05), 2611874T6 (LUNGTUT10)	722896X19C	(UTRSNOT05), 1571739X12 1), 4059114F6 (BRAINOT21
	Library	LATRTUT02	PENITUT01	BLADTUT04	BLADTUTO6	ADRENOT07	BRSTNOT19	SPLNNOT12	MONOTXT02	FIBPFEN06	HUVESTB01	SYNOOAT01	UTRSNOT05
	Clone ID	1405545	1451265	1556311	1901373	2367767	3090433	3800591	5308471	5324322	067184	722896	1571739
	Nucleotide SEQ ID NO:	<i>L</i> 9	89	69	02	71	7.5	73	74	75	91	7.1	78
	Protein SEQ ID NO:	1	2	ε	7	S	9	7	8	6	10	11	12

Table I (cont.)	tein Nucleotide Clone Library Fragments ID SEQ ID NO: ID	3 79 1739479 HIPONON01 511157H1 (MPHGNOT03), 511157T6 (MPHGNOT03), 1739479H1 (HIPONON01), 2092446T6 (PANCNOT04), 3880948F6 (SPLNNOT11)	80 1999147 BRSTTUT03 1339243T6 (COLNTUT03), 1999147H1 (BRSTTUT03), 3297709H1 (BRAITUT02), 2670959T6 (ESOGTUT02), 3297709H1 3396927H1 (UTRSNOT16), SCBA00828V1, SCBA00615 SCBA04646V1, SCBA01715V1, 5544151H1 (TESTNOC0	5 81 2182085 SININOT01 767764R6 (LUNGNOT04), 1655010F6 (PROSTUT08), 1701703T6 (BLADTLT55), 1871360F6 (SKINBIT01), 2081835F6 (UTRSNOT08), 2411644H1 (BSTMNON02)	6 82 2216640 SINTFET03 489759H1 (HNT2AGT01), 2057454T6 (BEPINOT01), 2097739H1 (BRAITUT02), 2216640H1 (SINTFET03), 2325135H1 (OVARNOT02), 2361273R6 (LUNGFET05), 2667958H1 (ESOGTUT02), 3462348H1 (293TF2T01), 3478754H1 (OVARNOT11), 4163069F6 (BRSTNOT32)	7 83 2417361 HNT3AZT01 1394742F1 (THYRNOT03), 2417361F6 (HNT3AZT01), 2417361H1 (HNT3AZT01)	84 2454384 ENDANOT01 2454384H1 (ENDANOT01), 2454384T6 (ENDANOT01), 2589653T6 (LUNGHOT022), 2643485F6 (LUNGTUT08), 2723048H1 (LUNGTUT10), 3130367H1 (LUNGTUT12)	9 85 2610262 LUNGTUT08 1226946R6 (COLNNOT01), 1226946T6 (COLNNOT01), 2610262F6 (LUNGTUT08)	0 86 2700075 OVARTUT10 604199R1 (BRSTTUT01), 1225126R1 (COLNTUT02), 1923323R6 (BRSTTUT01), 2301778R6 (BRSTNOT05), 2506882F6 (CONUTUT01), 2700075F6 (OVARTUT10), 2700075H1 (OVARTUT10), 2744960F6 (LUNGTUT11), 2833994F6 (TLYMNOT03), 2915413H1 (THYMFET03), 3647274H1 (ENDINOT01)	87 2786701 BRSTNOT13 754370R1 (BRAITUT02), 1426163R6 (BCDNGFET03), 1923562R6 (BRSTTUT01) 2215161T6 (SINTFET03), 2498589H1 (KIDNFET02), 3028991H1 (HEARFET02) 5065467H1 (ARTFTDT01)	12 88 3068538 UTRSNOR01 908465R2 (COLNNOT09), 957130R6 (KIDNNOT05), 1301520F6 (BRSTNOT07), 1580628H1 (DUODNOT01), 2631247F6 (COLNIUT15), 3068538H1 (UTRSNOR01), 3532286T6 (KIDNNOT25)	13 89 5159072 BRSTIWT02 412241R1 (BRSTNOT01), 660435H1 (BRAINOT03), 881160H1 (THYRNOT02), 1324073F1 (LPARNOT02), 2520427H1 (RPAINTMO1)
	Protein SEQ ID NO:	13	14	15	16	17	18	19	20	21	22	23

WO 01/05970 PCT/US00/19698

				() + orong
Protein SEQ ID	Nucleotide SEQ ID NO:	Clone	Library	Fragments
34	100	2590967	LUNGNOT22	2590967F6 (LUNGNOT22), 25 (COLANOT02), 3150287R6 (A
35	101	2824491	ADRETUT06	1381834X14 (BRAITUT08), 1381834X16 (BRAITUT08), 1381834X17 (BRAITUT08), 1381834X31 (BRAITUT08), 1972345F6 (UCMCL5T01), 2824491H1 (ADRETUT06), 3413970H1 (PTHYNOT04)
36	102	2825460	ADRETUT06	870873R6 (LUNGAST01), 1440326F1 (THYRNOT03), 2825460H1 (ADRETUT06), 2825460T6 (ADRETUT06), 4154518H1 (MUSLTWT01), 5068209H1 (PANCNOT23), SBLA03097F1
37	103	2871116	THYRNOT10	ທດ⊣ທ I
38	104	2942212	CONNTUTOS	Ð I
39	105	3685151	HEAANOT01	860843R1 (BRAITUT03), 1932207F6 (COLNNOT16), 1932207T6 (COLNNOT16), 2210580F6 (SINTFET03), 3043060H1 (HEAANOT01), 3685151H1 (HEAANOT01), 4960825H1 (TLYMNOT05)
40	106	4881515	UTRMTMT01	925415R1 (BRAINOT04), 1337450F6 (COLNNOT13), 1961288R6 (BRSTNOT04), 3581069H1 (293TF3T01), 3583842T6 (293TF4T01), 4881515H1 (UTRMTMT01), 5488514H1 (DRGTNON04), g1156606
41	107	5324681	FIBPFEN06	≘ ∄
2.	108	5387651	BRAINOT19	·2.5
43	109	5595679	COLCDITO3), 826501R1 (PROSNOTO6), 1251632X12 4F1 (PLACNOTO2), 1316814F1 (BLADTUT 3), 280615941 (BLADTUTO8), 2837021H 3H1 (BRSTNOT16), 3119883H1 (LUNGTUT 8), 3748742H1 (UTRSNOT18)
44	110	5782457	BRAXNOT03	532593R6 (BRAINOTO3), 532593T6 (BRAINOTO3), 5782457H1 (BRAXNOTO3)

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
45	111	760677	BRAITUT02	745006X13 (BRAITUT01), 760677H1 (BRAITUT02), 760677X19 (BRAITUT02), 763135X12 (BRAITUT02), 946075H1 (RATRNOT02), 953938H1 (SCORNON01)
46	112	1348567	PROSNOT11	1348567H1 (PROSNOT11), 1505075F6 (BRAITUT07), 1620627F6 (BRAITUT13), 2069105F6 (ISLTNOT01), 2417901F6 (HNT3AZT01), 2494683H1 (ADRETUT05), 3320166H1 (PROSBPT03)
47	113	1751354	LIVRTUT01	029909F1 (SPLNFET01), 029909R1 (SPLNFET01), 512371H1 (MPHGNOT03), 1439362F6 (PANCNOT08), 1751354F6 (LIVRTUT01), 1751354H1 (LIVRTUT01), 1900168F6 (BLADTUT06)
48	114	1976780	PANCTUT02	001347H1 (U937NOT01), 1755035X307D2 (LIVRTUT01), 1976780H1 (PANCTUT02), 2798389H1 (NPOLNOT01), 4050076H1 (SINTNOT18), 4228943H1 (BRAMDIT01), 4291877H1 (BRABDIR01), 5514957H1 (BRADDIR01), SCHA04173V1, SCHA02986V1, SCHA01162V1, SCIA02096V1
49	115	2048234	LIVRFET02	1553355F6 (BLADTUT04), 1929455F6 (COLNTUT03), 2048234H1 (LIVRFET02), 2699864T6 (COLNTUT10)
50	116	2111754	BRAITUT03	1335055F6 (COLNNOT13), 2105233R6 (BRAITUT03), 2111754H1 (BRAITUT03), 2111754R6 (BRAITUT03), 3706377H1 (PENCNOT07)
51	117	2123286	BRSTNOT07	411359F1 (BRSTNOT01), 411359R1 (BRSTNOT01), 708105R6 (SYNORAT04), 1322780F6 (BLADNOT04), 2123286H1 (BRSTNOT07), 2719651F6 (LUNGTUT10), 2880143F6 (UTRSTUT05), 3206153F6 (PENCNOT03), 3210501F6 (BLADNOT08), 3346625F6 (BRAITUT24), 3489118H1 (EPIGNOT01), 3605764H1 (LUNGNOT30), 4242993H1 (SYNWDIT01), 5089472H1 (UTRSTMR01)
52	118	2477507	SMCANOT01	488096H1 (HNT2AGT01), 1672690F6 (BLADNOT05), 1802830F6 (COLNNOT27), 1818538H1 (PROSNOT20), 2171841H1 (ENDCNOT03), 2477507H1 (SMCANOT01), 3434030F6 (PENCNOT05)
53	119	2759119	THP1A2S08	496782H1 (HNT2NOT01), 1251166H1 (LUNGFET03), 1289067F1 (BRAINOT11), 1295658T6 (PGANNOT03), 1510901F1 (LUNGNOT14), 1531583F1 (SPLNNOT04), 1533488F1 (SPLNNOT04), 1817447H1 (PROSNOT20), 2154846F6 (BRAINOT09), 2468875H1 (THYRNOT08), 2498852F6 (ADRETUT05), 2506652F6 (CONUTUT01), 2630812F6 (COLNTUT15), 2759119H1 (THP1AZS08), 2991227H1 (KIDNFET02), 3036646F6 (PENCNOT02), 3213032H1 (BLADNOT08)
54	120	2823818	ADRETUT06	(PGANNOT01), 2823818H1 ()

•		7
	_	ذ
	2	4
	Ξ	₹
	C)
		ì
`	_	_
		4
•		•
	-	•
	1	
_	1	2
•	_	┥
,	_	┥
*	_	┥
	2	┥

Protein SEQ ID NO:	Nucleotide SEQ ID NO:	Clone ID	Library	Fragments
55	121	2859730	SININOTO3	103901X6 (BMARNOT02), 510695H1 (MPHGNOT03), 1452088H1 (PENITUT01), 1527095F6 (UCMCL5T01), 2285371H1 (BRAINON01), 2843029H1 (DRGLNOT01), 2859730H1 (SININOT03)
95	122	2861155	SININOTO3	875215T1 (LUNGAST01), 999673H1 (KIDNTUT01), 1425091R6 (BEPINON01), 2861155F6 (SININOT03), 2861155H1 (SININOT03), 2901915F6 (DRGCNOT01), 3621947H2 (ENDANOT03)
57	123	3002667	TLYMNOT06	227882F1 (PANCNOT01), 227882R1 (PANCNOT01), 260725H1 (HNT2RAT01), 1432542R1 (BEPINON01), 2474761F6 (SMCANOT01), 3002667H1 (TLYMNOT06), 3188977H1 (THYMNON04), 3461163H1 (293TF1T01), 4860339F6 (PROSTUT09)
58	124	3043734	HEAANOT01	3043734H1 (HEAANOT01), 3043734T6 (HEAANOT01), 3209823H1 (BLADNOT08), 5277071H1 (MUSLNOT01)
29	125	3294893	TLYJ INTO1	389234H1 (THYMNOTO2), 1242886H1 (LUNGNOTO3), 1539958T1 (SINTTUTO1), 1870567H1 (SKINBITO1), 2069284F6 (ISLTNOTO1), 2280217R6 (PROSNONO1), 2353465T6 (LUNGNOT20), 2798990F6 (NPOLNOTO1), 3180440H1 (TLYJNOTO1), 3294893H1 (TLYJNTO1), 3816962H1 (TONSNOTO3), 5039889H2 (COLHTUTO1), 5118831H1 (SMCBUNTO1)
09	126	3349052	BRAITUT24	731775H1 (LUNGNOTO3), 1449575H1 (PLACNOTO2), 1899442F6 (BLADIUTO6), 1967162T6 (BRSTNOTO4), 2630025F6 (COLNTUT15), 2717821H1 (THYRNOTO9), 3180478T6 (TLYJNOTO1), 3349052H1 (BRAITUT24), 4523961F6 (HNT2TXT01), 5565623H1 (TLYMNOTO8), 6141909H1 (BMARTXTO3)
61	127	3357264	PROSTUT16	2378150F6 (ISLTNOT01), 2378150X304B1 (ISLTNOT01), 2378150X304D1 (ISLTNOT01), 2807493F6 (BLADTUT08), 2881251F6 (UTRSTUT05), 3357264F6 (PROSTUT16), 3357264H1 (PROSTUT16), 3593272H1 (2937F5T01), 4163652T6 (BRSTNOT32), 4821588F6 (PROSTUT17), 4872125H1 (COLDNOT01)
62	128	3576329	BRONNOT01	1444072F6 (THYRNOT03), 1649584T6 (PROSTUT09), 1720770X15C1 (BLADNOT06), 1720770X16C1 (BLADNOT06), 2204612F6 (SPLNFET02), 3576329H1 (BRONNOT01), SAFC01083F1
63	129	3805550	BLADTUT03	1416364F6 (BRAINOT12), 1553473H1 (BLAD/TUT04), 3232384H1 (COLNUCT03), 3287257H1 (HEAONOT05), 3539473H1 (SEMVNOT04), 3805550H1 (BLAD/TUT03)

Table 1 (cont.)

Protein SEQ ID NO:	Protein Nucleotide SEQ ID SEQ ID NO: NO:	Clone ID	Library	Fragments
64	130	4546403	COLXTDT01	4546403 COLXTDT01 1687704F6 (PROSTUT10), 1962744R6 (BRSTNOT04), 2674742F6 (RIDNNOT19), 4546403H1 (COLXTDT01), 4632828T6 (GBLADIT02)
9	131	4767318	BRATNOT02	4767318 BRATNOT02 134566R1 (BMARNOT02), 549352R1 (BEPINOT01), 1819757T6 (GBLATUT01), 2863295H1 (KIDNNOT20), 4767318H1 (BRATNOT02), SBLA03778F1, g3737930
99	132	4834527	BRAWNOT01	859906X38C1 (BRAITUTO3), 1231225H1 (BRAITUTO1), 1393681T6 (THYRNOTO3), 1416996F6 (BRAINOT12), 2422475H1 (SCORNONO2), 3999137R6 (HNT2A2SO7), 4834527F6 (BRAWNOTO1), 4834527H1 (BRAWNOTO1), 5691642H1 (BRAUNOTO2)

Table 2

Analytical Methods & Databases	BLAST-Genbank BLAST-DOMO MOTIFS	ProfileScan MOTIFS BLIMPS-PRINTS HWMER-PFAM SPSCan	BLAST-Genbank	BLAST-Genbank MOTIFS HWMER-PFAM BLIMPS-BLOCKS BLIMPS-PRINTS BLAST-DOMO	BLAST-Genbank HWMER-PFAM ProfileScan BLIMPS-PRINTS	BLAST-Genbank SPScan
Homologous Sequences	GTP-binding protein; CgpA [Caulobacter crescentus] g3820578		Ras inhibitor [Homo sapiens] g190895	Small GTP binding protein [Saccharomyces cerevisiae] g1171484	Similar to WD domain, G-beta repeat protein [C. elegans] q3880929	Rabin3 (Rattus norvegicus) g624225
Signature Sequences, Motifs, and Domains	GTP-binding protein: D79-M234, Y80-C239 ATP/GTP binding site (P- loop): G102-S109	Beta transducin family, G-beta repeats: T269-L315 , F261-D293 L280-V294 , V185-V199 Signal peptide: M1-A35		ATP/GTP-binding site: G28-S35 Ras family: K23-T219 Ras transforming protein: V22-M43, A63-S85, P124-A137, L156-A178, D102-S145, K150-S180	WD domain, G-beta repeats: M1-T64, M27-K41, F274-K306	Signal peptide: M1-A57
Potential Glycosylation Sites	N12		N125 N354 N445	N111 N140 N198	N149 N287 N327 N351	N270 N350
Potential Phosphorylation Sites	S59 T71 T146 T211 T73 S127 T133 S216	S59 S188 S200 S284 S367 S381 T399 T29 T193 T288 T354 S419	S151 S152 T443 T444 S33 S104 S126 S127 S135 S216 S239 T350 T383 S450 T481 S146 T223 S287 S356 T434 T470	T108 S153 S9 S160 S215 T219 T142 S180	T108 S360 S115 T217 T264 S295 S296 S35 S52 S160 S174 T206 T249	T18 T107 T123 S149 S199 S280 S336 S369 S71 T106 S387 Y302 Y400
Amino Acid Residues	269	428	562	229	360	460
SEQ ID NO:	1	7	m	4	ر.	9

_	
_	
. :	
$\overline{}$	
$\mathbf{\mathcal{C}}$	
8	
\cdot	
$\overline{}$	
\sim 1	
(1)	
e 2	
ble	
ble	

SEO	Amino	Potential	Potential	Signature Seguences,	Homologous	Analytical
â	Acid	Phosphorylation	Glycosylation	Motifs, and Domains	Sednences	Methods &
NO:	Residues	Sites	Sites			Databases
7	239	25	N188	Phosducin:	Phosducin-like	BLAST-Genbank
		198 TI		L20-I179, S25-I179,	protein [Homo	BLAST-PRODOM
		T206 S236 S223		E30-D239	sapiens) g4104075	BLAST-DOMO
æ	334	T225 T235 S260		ATP/GTP-binding site (P-	GTP-binding	BLAST-Genbank
		T4 S45 S63 S133		loop): G150-S157	protein homolog	MOTIFS
		S162 S193 T279		GTP1/0BG family:	[L. braziliensis]	BLIMPS-BLOCKS
		T308		L75-D89, I146-Q166	g2570231	BLIMPS-PRINTS
				G-protein, alpha		
				subunit: I79-L87		
6	341	S91 T122 S185		Signal peptide:	Putative WD-40	SPScan
		T228 S		M1-A61	repeat protein	BLAST-Genbank
		T85 S323		WD domain, G-beta	(Arabidopsis	MOTIFS
				repeats:	thaliana] g4191773	ProfileScan
				L164-D196, C173-P217,		HMMER-PFAM
						BLIMPS-BLOCKS
						BLIMPS-PRINTS
10	513	T72 T10	N242 N417	Beta-transducin family,	Similar to WD	BLAST-Genbank
		S124 S136 S215		G-beta repeats:	domain G-beta	MOTIFS
		Η.		F345-N377, K210-N242,	repeats protein	HMMER-PFAM
		-			[C. elegans]	BLIMPS-BLOCKS
		S338 T372 T386		N353-V400, L229-F243,	g3875246	BLIMPS-PRINTS
		S437 S451 T473		I364-M378		ProfileScan
1	186	TK1 CR0 C107	M64 N148	ARE-family.	Similar to ADD-	RI.AST-Conhank
:)	831 TES		N6-5186 D51-590		HWINER DEAM
					factor [C	RLTMPS-RIOCKS
				CTD-binding Cap1	eleganel m3881189	BI.TMDG-DBINTG
				protein:		MOTIFS
				F78-K103, I123-I144		
	ı			ATP/GTP binding site (P-		
				loop): G27-T34		

SEQ	Amino	Potential	Potential	Signature Sequences,	Homologous	Analytical
NO:	Acid Residues	Fnosphorylation Sites	Glycosylation Sites	Motils, and Domains	Sequences	Methods & Databases
12	204	S184 S203 S34 S152 T14 T20		Ras family: K5-M189 Ras transforming	Ras-like protein,	BLAST-Genbank HMMER-PFAM
		r62	•	protein:		BLIMPS-PRINTS
				M1-E150, V4-T25,		BLAST-DOMO
						MOTIFS
				ATP/GTP binding site (P- loop): G10-S17		
13	100	S31 S46 T52 T61		Beta-transducin, WD	Similar to beta-	BLAST-G nbank
		S4 S26 S		repeats:	transducin (C.	MOTIFS
		9.B.L		L81-M95, V70-S100,	elegans] g3875373;	BLIMPS-BLOCKS
				OOTS-TW	Alzhelmer's	ProfileScan
					disease protein	BLIMPS-PRINTS
					[Homo sapiens] Genesed W21578	BLAST-PRODOM
14	795	T569 S776 S54	NS2 N421 N559	WD domain, G-beta	Phospholipase A2-	RLAST-Genhank
		S188 S201 T248	N708		activating protein	BLAST-PRODOM
		T249 T298 S306		,139,	Rattus	BLAST-DOMO
		S368 T422 S466			Norvegicus]	HMMER-PFAM
		TS61 S586 S625		L126-N140, M166-A180	g1017706	BLIMPS-BLOCKS
		S678 T/31 S/77				BLIMPS-PRINTS
		777 T#7 7770				
		T134 T1/4 S213				
		1756 S391				
		S415 S588 S620 S694 T742				
12	393	S48 S61 T143	N182 N197	WD domain, G-beta	Putative WD-repeat	BI.AST-Genbank
		T148 T20	•	repeats:		HMMER-PFAM
		T212		L121-A153, L357-R389,	Arabidopsis	ProfileScan
		S266 S325		P322-F369, L140-S154	thaliana] q4263521	BLIMPS-PRINTS
16	485	S31 S108 S222		Beta-transducin, WD		BI.AST-Genbank
		S321 S346 S357		repeats:	(Xenopus laevis)	MOTIFS
		T84 T125 T137		L129-L143, V219-T233,	g3687833	HMMER-PFAM
		T151 T187 S227				ProfileScan
		1.268 8395 T403		L429-V443, L452-G468		BLIMPS-BLOCKS
		2407 T457 X92				BLIMPS-PRINTS
		1021				BLAST-DOMO
						BIAST-PRODOM

	_	
•	ئ	;
	Ξ	
	ဥ)
	_	
`	_	_
(<u> </u>	
(e 2 (
` -	<u>د</u>	
`	•	

Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs, and Domains	Homologous · Sequences	Analytical Methods & Databases
	T32 T91 S177 T56 S153 S186 Y149		ATP/GTP-binding site (P- loop): G15-T22 Transforming protein, p21: L9-H30, T32-K48, I50-S72, Q115-L128, Y149-A171 Ras protein: K5-E151	Rab7 [Mus musculus] g1050551	BLAST-Genbank MOTIFS BLIMPS-PRINTS BLAST-PRODOM BLAST-DOMO
	T18 T46 S120 S5 T151 T83 S125	N81 N159		Rhotekin [Mus musculus] g1293145	BLAST-Genbank
	SS6 S84 T234 S41 T91 T132 T234 T11 T47 T80 T194	N89 N188	Beta-transducin, WD- repeats: S41-W51, F195-D227, L238-N270, L214-1228, L257-M271, T203-S249	10 4 00 4 2 2	BLAST-Genbank MOTIFS HWMER-PFAM BLIMPS-BLOCKS ProfileScan BLIMPS-PRINTS BLAST-PRODOM
	T277 T364 S393 S448 S479 S483 T554 T568 S586 S239 S250 T374 S379 T398 S485 T528	N274	Beta-transducin, WD- repeats: L390-L404, L370-D403, L413-R445	Similar to WD domain G-beta repeat prot. [C. elegans] g3880340; 70kD tumor- specific antigen [R. norvegicus] g2505957	BLAST-Genbank HWMER-PFAM BLAST-PRODOM BLAST-DOMO BLIMPS-BLOCKS BLIMPS-PRINTS
1:	T426 S451 S28 S51 T81 T89 T166 S214 T241 S264 T305 S343 S185 T193 S421	N58	ATP/GTP-binding site (P- loop): G73-S80 Cell division control protein: V47-P240	Similar to Drosophila melanogaster septin (sep2) [Homo sapiens] g1503988	BLAST-Genbank BLAST-PRODOM BLAST-DOMO MOTIFS
	S169 T239 T292 S309 S382 S129 S297 Y60 Y101 Y315	N338	Protein GTPase activating protein: L8-S169 PH domain: Y138-Q355, Q191-I351, P210-E375	RhoGAP protein (Homo sapiens) g312212	BLAST-Genbank BLAST-PRODOM BLAST-DOMO

				(
SEQ ID NO:	Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs, and Domains	Homologous Sequences	Analytical Methods & Databases
23	406	T83 S143 S303 T75 T115 T126 T211 S216 T289 T315 Y247	N184 N401 N402		Rab 9 effector, P40 [Homo sapiens] g2217970	BLAST-Genbank
24	229	S7 S127 T50 S178		ATP/GTP-binding site (P- loop): G40-T47 Ras family: K35-L217 Transforming protein, p21: F34-A55, R57-R73, V75-K97, N139-L152	Rab GTPase, Rab33B [Mus musculus] g2516239	BLAST-Genbank MOTIFS HWMER-PFAM BLIMPS-PRINTS BLAST-DOMO
25	670	T28 T45 S69 S3 S108 T277 S406 S6 T52 T82 S91 S102 S126 S609 S158 S197 T213 S217 T281 S323 S416 T419 T428 T474 S496 T540	N343	G-beta WD repeat domain: F386-D424, L411-T425, Y429-D465, L469-D504, L510-D545, L549-D585, K589-S629, M633-T669 Beta-transducin Trp-Asp repeats signature: C401-I447	Beta transducin- like protein [Podospora anserina] g607003	BLAST-GenBank BLIMPS-BLOCKS BLIMPS-PRINTS HWMER-PFAM MOTIFS ProfileScan
26		T17 T48 T126 T160 T293 T364 T97 T132 S201 S217 S305 T322 S357 S434 Y339	N46 N95 N355	G-beta WD repeat domain: L62-N95, V82-L96, F124-M138, F297-V311 Beta-transducin Trp-Asp repeats signature: S316-A356 SOF1 protein, WD repeat: D129-V277, F309-V444	Beta-transducin [Schizosaccharomyc es pombe] g3393019	BLAST-GenBank BLAST-DOMO BLAST-PRODOM BLIMPS-BLOCKS BLIMPS-PRINTS HMMER-PFAM
27	236	S24 S60 S86 T181 S117 S140		<pre>GYP7, GTPase activating protein: M1-I155</pre>	GTPase activating protein [Yarrowia lipolytica]	BLAST-GenBank BLAST-PRODOM MOTIFS

	_	_
•		_
	_	ڏ
	Ē	-
	•	•
	Ç)
	ح	ì
	`	٠
1	_	
		ì
ţ	٠,	4
	_	
	٩	J
۲	_	-
	c	כ
•	2	₹
,	•	•

			70		
	Forencial	Forential	Signature sequences,	HOMO TORON	Minigue
Acid Residues	Phosphorylation Sites	Glycosylation Sites	Motits, and Domains	Sednences	Methods & Databases
	1158		G-beta WD repeat domain:	Similarity to	BLAST-GenBank
	S47		L188-Q220, L446-G479,	guanine nucleotide	BLIMPS-BLOCKS
	T8 7		M466-P480	binding protein	BLIMPS-PRINTS
	T355 T474 Y239		Beta-transducin Trp-Asp	[Caenorhabditis	HMMER-PFAM
			repeats signature:	elegans] g3878300	MOTIFS
			F200-A245		ProfileScan
	S63 S104 S148	N265	G-beta WD repeat domain:	Similar to guanine	BLAST-GenBank
	S189 T208 S276		L41-G73, I83-D115,	nucleotide binding	BLAST-PRODOM
	S50 T110 S118		L102-V116, L125-D157,	protein	BLIMPS-BLOCKS
	T124 S152 T160		L167-D199, I210-D242	Caenorhabditis	BLIMPS-PRINTS
	T237 T326		Beta-transducin Trp-Asp	elegans] g3874290	HMMER-PFAM
			repeats signature:		MOTIFS
			S49-A308		ProfileScan
			Signal peptide: M1-A47		SPScan
	S102 T145 S188	N209	Protein with WD repeat:	F-box protein	BLAST-PRODOM
	S52 T89 S204		P7-W129		BLAST-GenBank
	S222 S283		Signal peptide:	musculus] g6456114	MOTIFS
			M1-S68		SPScan
	r13	N159	Ò.	TipD (sequence	BLAST-GenBank
	T161 T1			similarity to	BLAST-PRODOM
	S285 T3			Beta-transducin	BLIMPS-BLOCKS
	S432 T4		E460-D497, T506-S543,	family)	BLIMPS-PRINTS
	S 213		G547-A586	(Dictyostelium	HMMER-PFAM
	S394 T4		Beta-transducin Trp-Asp	discoideum]	MOTIFS
	T546		repeats signature: A308-E354, L393-Q441	g2407788	ProfileScan
	r84 S	N187	G-beta WD repeat domain:		BLIMPS-BLOCKS
	S142 T261 T65		L120-N153, I140-L154		BLIMPS-PRINTS
	T148 T178 T189				HMMER-PFAM
	1221				MOTIFS
	T157 T218 T248 S320 S347 S412	N59 N225	G-beta WD repeat domain: D180-E211 A198-V212		BLIMPS-BLOCKS BLIMPS-PRINTS
	S7 T236 S290				HMMER-PEAM
	T396 T406 Y63				MOTTES

•		-
•		5
(•	•
	9	5
_	c	J

Γ		쏙	ች ⁻ 8 8	្រន	λc. μ
	Analytical Methods & Databases	BLAST-GenBank BLAST-PRODOM MOTIFS	BLAST-GenBank BLAST-DOMO BLAST-PRODOM BLIMPS-BLOCKS BLIMPS-PRINTS HMMER-PFAM MOTIFS ProfileScan	BLIMPS-PRINTS MOTIFS SPScan	BLAST-GenBank BLAST-DOMO BLAST-PRODOM HWMER MOTIFS
	Homologous Sequences	DMR-N9 (homology to WD repeat sequences) [Mus musculus] g817954	eRFS (related to eukaryotic release factor 3) [Mus musculus] g4566435		Hypothetical trp- asp repeats containing protein [Schizosaccharomyc es pombe] g3850059
	Signature Sequences, Motifs, and Domains	DMR-N9 protein: K93-S148	ATP/GTP-binding site motif A (P-loop): G267 Elongation factor 1 alpha protein (GTP-binding) domain: D485-E684 Elongation factor Tu domain: K258-D658, N262-K273, M343-G374, R664-G677 GTP-binding elongation factors signature: A249-E420, N262-T275, K294-P346, T341-F351, T357-V368, L401-Q410, P443-I682	G-beta WD repeat domain: V146-L160, L284-I298 Signal Peptide: M1-T56	Beta-transducin Trp-Asp repeats signature: N101-L162 Trp-Asp repeats- containing protein: R54-A172 Transmembrane domain:
	Potential Glycosylation Sites		N526 N621	N32	
	Potential Phosphorylation	T137 T18 T102 Y96	T173 S25 S43 S74 S83 S127 S152 S154 S182 T316 T331 T341 S372 T535 T606 S623 T138 T151 S168 S238 S299 T336 T422 S476 T506 T530 T628	S342 T52 S71 T102 T119 T224 T324 T6 S195 S271 T353 X225	S183 T.
٠	Amino Acid	161	684	366	339
	SEQ ID	34	3.5 3.5	36	37

_
つ
nt
8
\mathcal{O}
_
\sim
Ø
=
9
੍ਰਕ
Ta

Analytical Methods & Databases	BLAST-GenBank BLAST-DOMO BLAST-PRODOM BLIMPS-PRINTS HMMER-PFAM MOTIFS SPSCan	BLAST-GenBank BLIMPS-BLOCKS BLIMPS-PRINTS HMMER-PFAM MOTIFS	BLAST-GenBank BLAST-DOMO BLAST-PRODOM BLIMPS-PRINTS MOTIFS	BLAST-Genbank BLIMPS-BLOCKS BLIMPS-PRINTS HMMER-PFAM MOTIFS SPScan
	Rab-related GTP- Ibinding protein [Homo sapiens] g1491714	similar to beta- transducin [Caenorhabditis elegans] g860695	Gtr2 homolog, novel small GTPase subfamily [Schizosaccharomyc es pombe] g3560242	Putative transcriptional regulation protein, trp-asp repeat containing [Schizosaccharomyc
Signature Sequences, Motifs, and Domains	ATP/GTP-binding site motif A (P-loop): G15 GTP-binding protein signature (Arf1, Ran): W5-E179 Ras family signature: R10-C213 Transforming protein p21: F9-E30, R32-R48, E51-S73, Y114-L127, Y149-I171	G-beta WD repeat domain: C-beta WD repeat domain: L93-D69, K73-D110, L97-A111, W114-N152, L236-K276, I263-L277 Signal peptide: M1-T43	ATP/GTP-binding site motif A (P-loop): G68 G-protein alpha subunit: R63-Q78 GTP-binding protein GTR1: A57-D294 Ras transforming protein: K61-L203	3-beta WD repeat domain: C184-E217, L204-Y218 Signal peptide: M1-G18
Potential Glycosylation			N88 N106 N321 N322	N3 67
Potential Phosphorylation	T29 T134 S153 T181 S200 T92 T129 S207	S209 T363 S60 S99 S119 S135 T144 T147 S174 S210 T350 S359 S370 T371	S86 T191 S219 S224 S254 S275 S308 S59 S72 T96 S373 S385 T394	T106 S337 S391 S29 S30 S41 S130 S154 S207 S231 S326 S82 S97 T212 S220
Amino Acid	213	393	399	412
SEQ	38	39	40	41

	_	
1	. :	•
•	☱	
	_	
	ဗ	
`	\simeq	•
(N	
(7 6	
•	<u>မ</u>	
•	ple	
•	<u>မ</u>	

SEQ	Amino	Potential	Potential	Signature Sequences,	Homologous	Analytical
NO:	Acid Residues	Phosphorylation Sites	Glycosylation Sites	Motifs, and Domains	Sequences	Methods & Databases
42	163	S15 S17 S71 T114 Y49			Arf-like 2 binding protein BART1 [Homo sapiens] g4426962	BLAST-GenBank MOTIFS
43	514	S113 T174 S263 S297 S441 S484 S510 T100 S192 T371 T490 Y255		G-beta WD repeat domain: L204-Q236, L462-G495, M482-P496 Beta-transducin Trp-Asp repeats signature: F216-A261	Similarity to guanine nucleotide binding protein [Caenorhabditis elegans] g3878300	BLAST-GenBank BLIMPS-BLOCKS BLIMPS-PRINTS HMMER-PFAM MOTIFS
44	67	T30 S15 Y18		C-protein gamma subunit: E2-L67, M9-R24, K10-P57, D45-G62 Prenyl group binding site (CAAX box): V64	G gamma protein [Mus musculus] g7259257	BLAST-GenBank BLIMPS-BLOCKS BLIMPS-PRINTS HMMER-PFAM
45	315	T148 S162 S209 S244 S252 S45 T48 S132 S140 S158 T214 S244	N7 9	WD40 domains/G-beta repeats: Q15-N53, G57-N95, G99-D137, P143-D179, G223-D263 WD/G-beta profiles: L71-Q116, T114-V161 WD/G-beta repeat signature: V250-L264	Contains similarity to G beta repeats (PROSITE:PS00670) of the beta- transducin family [Caenorhabditis elegans] g1086900	BLAST-GenBank MOTIFS ProfileScan HMMER-PFAM
46	504	T268 T99 T193 S323 S324 T409 T493 T91 T98 T133 T185 T234 T259 T264 T287 T337 S415 S498	N37 N295	WD40 domains/G-beta repeats: A211-D250, E254-S292, A296-A331, G338-D378, R382-D420 WD/G-beta profiles: T396-1442, T268-A316, C355-F400 WD/G-beta signatures: L407-L421, V279-V293 WD repeat protein-like region: I4-A226	Similar to S. cerevisiae PRP19 protein; simliar to G-beta repeat region of guanine nucleotide binding protein [Caenorhabditis elegans] g727450	BLAST-GenBank BLAST-PRODOM MOTIFS BLIMPS-PRINTS ProfileScan HMMER-PFAM

_	_
	-
-	ٽ
Ċ	:
7	5
>	<u>ر</u>
٠,	J
_	_
\ddot{c}	_
C	1
_	1
C	1

Amino Acid Residues	Potential Phosphorylation Sites	Potential Glycosylation Sites	Signature Sequences, Motifs, and Domains	Homologous Sequences	Analytical Methods & Databases
	S31 S1 S1 S1 S3 S3 S3 S3 S3 S3 S3 S3 S3 S3 S3 S3 S3	N226 N355		SAPK (stress activated protein kinase) interacting protein (similar to ras inhibitor) [Gallus gallus]	BLAST-GenBank MOTIFS
	T109 S27 S86 S188 S7 S8 S82 T96 T105	N29 N136 N186	Pleckstrin homology (PH) domains: S3-N45, I59-Q301 RhoGAP domain: P140-N291 GTPase protein-like region: G125-L307	Beta2-chimaerin [Homo sapiens] g457230	BLAST-GenBank BLAST-PRODOM BLAST-DOMO HMMER-PFAM MOTIFS BLIMPS-PRINTS BLIMPS-PRODOM
	S97 S199 T249 S342 S369 S382 T54 T182 T381		ATP/GTP-binding site motif (P-loop): G155-S162 GTP1/OBG GTP-binding protein family signatures: V151-A171, K172-1190, V200-G215, G217-D235 GTP-binding protein-like region: F15-P173 RAS transforming protein-like L145-L296	GTP-binding protein [Aquifex aeolicus] g2984292	BLAST-GenBank BLAST-PRODOM BLAST-DOMO BLIMPS-BLOCKS BLIMPS-PRINTS MOTIFS

`نب
Ţ
္ပ
\mathcal{L}
0
به
Ξ
Ta

Amino Potential Potential Acid Phosphorylation Glycosylation	1 tion	Potential Glycosylation		Signature Sequences, Motifs, and Domains	Homologous Seguences	Analytical Methods &
es Sites		Sites	_		1	Databases
T308 S65	T308 S65 N108			ATP/GTP-binding site	NOEY2 putative	BLAST-GenBank
T262 S34 S81	524 T228 S34 S81	N 3 6 6		G149-S156	[Homo sapiens]	BLAST-DOMO
T262	T262 S2			Ras domain: R144-M334	g4100355	HMMER-PFAM
				p21/ras-related		BLIMPS-BLOCKS BLIMPS-PRINTS
			_	gidnatures.		MOTIFS
				Y143-S164, N166-L182,		
			_			
	<u> </u>	<u> </u>	<i>(</i> 2,	Ras transforming		
				protein-like region:		
		•	<u>.</u>	I140-E284		
2 N133 N148	S38 T62 N133 N148	N148	Y.	Regulator of chromosome	UVB-resistance	BLAST-GenBank
(116 S169 N179 N293	(116 S169 N179 N293	N293	<u>ပ</u>	condensation (RCCI)/	protein UVR8	BLAST'- PRODOM
T379 S421 N296	T379 S421 N296		0	guanine nucleotide	[Arabidopsis	HMMER-PFAM
S456 S12	S456 S12	ਚ <u>'</u>	<u>ರ</u> '	dissociation stimulator	thaliana) g5478530	PROFILESCAN
3150 T366	3150 T366	70	Ö			BLIMPS-PRINTS
T482 Y	T482 Y			E117-S169, D170-D222,		MOTIFS
X449	X449	•		T223-D274, E275-G292,		
			_	G328-G339		
<u>к</u>	ж.	<u>~</u>	<u>~</u>	RCC1 signatures: V157-L167, V262-L272		
T230 S266 N76	T230 S266 N76		3	WD40 domains/G-beta	Sec13-related	BLAST-GenBank
522	S19 S22	<u> </u>	ч	repeats:	protein	HMMER-PFAM
S240	S240			Q33-R73, W79-T119,	Arabidopsis	PROFILESCAN
		•		W126-K181, W188-T230,	thaliana g3150415	BLIMPS-PRINTS
				P241-K276, S11-A50		BLAST-PRODOM
		0,	-	Sec13 related/WD repeat		MOTIFS
				protein-like region:		
1	•		_	R73-1177		
<u> </u>	<u>~</u>	3	3	WD/G-beta profile:		_
				G11-A50		

WO 01/05970 PCT/US00/19698

	sequences mernous & Databases	HMMER-PFAM	BLIMPS-PRINTS	MOTIFS							GTP-binding BLAST-GenBank	protein (Bos HHMER-PFAM	taurus) g162764 BLIMPS-PRINTS	BLAST-DOMO	BLAST-PRODOM	MOTIFS								musculus] g4895039 HMMER-PFAM	BLAST-PRODOM	BLAST-DOMO	MOTIFS					nucleotide-binding HMMER-PFAM	protein beta 5 BLIMPS-PRINTS	[Mesocricetus MOTIFS	
Signature Sequences,	יייים בייים אווס המונים	WD40 domains/G-beta		V199-K237, V248-S284,	G287-H326	Drosophila lethal(2)	giant larvae tumor	suppressor protein	signature:	K221-P244, A353-E377	site	7-T44	Ras family domain:	K32-C227	p21/ras-related	transforming protein		V72-T94, D134-M147,	_	Ras transforming	protein-like region:	F27-T172	WD40 domains/G-beta Co		D70-Q109, T120-N159,		G-bera repeat signature: L146-V160	WD repeat/coronin	protein-like region:	I208-Q467	ains/G-beta		, C312-A353, 1		
Potential Glycosylation	Sites	N114	•								N38			-									N179 N185									N14/ N29/			
Potential Phosphorylation	Sites	S206 S514 T22	T226		TISS	T350	2609	S913	Y862		T113	T155 S173												\$450 S	S130 T1	822	20%			1	S16 T// S85 S90	2114	T166	244	
Amino	Residues	949									227												474								7 5 5				
SEQ	ë	23									54												22							7	90	_		_	

$\overline{}$
نید َ
on
ತ
ā
<u>(b</u>
回
ਢ

F						
	Analytical Methods & Databases	BLAST-GenBank PROFILESCAN HMER-PFAM	BLAST-GenBank MOTIFS	BLAST-GenBank MOTIFS	BLAST-GenBank HMMER-PFAM BLIMPS-BLOCKS BLIMPS-PRINTS ProfileScan BLAST-PRODOM BLAST-DOMO MOTIFS	BLAST-G nBank MOTIFS
	Homologous Sequences	Beta-transducin- like protein [Podospora anserina] g607003	HP protein (RhoGAP ortholog) [Homo sapiens] g2559002	GTPase activating protein [Schizosaccharomyc es pombe] g3150248	Elongation factor G [Rattus norvegicus] g310102	Rho target rhophilin [Mus musculus] g1176422
	Signature Sequences, Motifs, and Domains	G-beta profile: S106-S152		Amino acyl tRNA ligase motif: P173-T183	GTP binding elongation factor Tu family domain: E44-T530 Elongation factor G C-terminus domain: L556-T727 GTP binding elongation factor signatures: N48-T61, Q97-A105, N117-F127, R133-V144, F169-R178	
	Potential Glycosylation Sites	N26 N44 N271 N424 N628		N71 N108 N381	N344 N640	N75 N582
	Potential Phosphorylation Sites	T331 S431 T637 S34 S169 S554 S28 S124 S192 S273 S341 T366 S426 S449 S470	S15 T2 S3 T24	S63 S223 T64 T117 S147 S159 S195 S200 T214 S271 S401 S448 T49 S110 S195 T235 T280 T439	T287 S543 T61 S275 S345 T430 T474 T565 T676 S705 S726 T727 S57 T63 T70 T287 S345 T389 T432 S458 T479 T518 T538	T492 S615 S619 T35 S142 T177 T212 S224 S270 T353 S403 T456 T471 T500 T550 S560 S572 T378 S403 S496
	Amino Acid Residues	989	6	521	. 751	999
	SEQ ID No:	57	58	53	09	61

_
_
•
_
\Box
=
Ō
\sim
$\ddot{\circ}$
. •
$\overline{}$
$\overline{}$
\sim
<u>~</u>
7
e 2 (
<u>e</u>
<u>e</u>
ble
<u>e</u>

0.00	(is ; is a	Dotostial	Dotontial	gimature Semiences	Homologous	Analytical
JEZ ID	Acid	Phosphorylation	GI	Motifs, and Domains	Sednences	Methods &
NO:	Residues	Sites				Databases
62	746	S22 T98 S571		WD40 domains/G-beta	Bop1 growth	BLAST-GenBank
		S53 S61		repeats:	control protein	BLAST-PRODOM
		S71 T97		T403-E441, R570-H606,	[Mus musculus]	BLAST-DOMO
		S127 T1		Q610-D648, T653-H691,	g1679772	MOTIFS
		T190 S2		L704-T746, C418-A461		BLIMPS-PRINTS
		S279 S323 S430		G-beta repeat signature:		ProfileScan
		S680 S7		L428-V442		HMMER-PFAM
		T190 T2		Trp-Asp repeat protein-		
		S436		like region: S22-L407		
63	212	S105 S142 S148	N131	ATP/GTP-binding site	Rab19 [Mus	BLAST-GenBank
		S162 S167 S44		motif (P-loop): G25-T32	musculus] g2598565	HMMER-PFAM
		T56 T101 S162		Ras family domain:		BLIMPS-BLOCKS
				K20-C212		BLIMPS-PRINTS
				ADP-ribosylation factor		BLAST-DOMO
				family domain: P6-R183		BLAST-PRODOM
				p21/ras-related		MOTIFS
				transforming protein		
				signatures:		
				F19-T40, A42-K58,		
				L60-T82, S122-L135,		
				A158-L180		
				Ras transforming		
				protein-like region:		
				X15-I155		

·
آت َ
<u>(</u> 2)
$\mathbf{U}_{\mathbf{U}}$
$\overline{}$
7
e 2 (
le

				Homol oxoll	Analytical
Potential Phosphorylatic	, L	Potential	Signature sequences, Motifs, and Domains	Sequences	Methods &
Sites	•	Sites			Databases
T275 S276 T15	Γ	N196 N291	WD40 domains/G-beta	Hypothetical trp-	BLAST-
S25 T99 S164			repeats:	asp repeats	SwissProc
S201 S6 S270			M1-149, L60-D98,	protein [C.	HMMER-PFAM
T293			E102-Q140	elegans] SwissProt	BLIMPS-PRINTS
			Sterile alpha motif	293847	Profil Scan
			(SAM): E161-R225		MOTIFS
			WD/G-beta signatures:		
			L36-V50, L127-F141		
			G-beta profile:		
			L74-P122		
S137 T167 T193			WD40 domains/G-beta	WD repeat protein	BLAST-GenBank
S202 S237 S276			repeats:	[Schizosaccharomyc	HMMER-PFAM
S290 S310 S362			H72-L110, L116-D155,	es pombe] g5701965	ProfileScan
S82 T150 T158		_	L241-D279		MOTIFS
T199 S362 T368			G-beta profiles:		
			S137-C175, S87-C133,		
			I255-S312		
S6 T24 S69 T209		N448	RasGEF domain: V197-E397	Putative guanine-	BLAST-GenBank
S357 T4			Guanine nucleotide	nucleotide	HMMER-PFAM
S181 S236 S242			releasing protein-like	releasing factor	BLAST-PRODOM
T322 T407 T450			region: P201-S432	[Drosophila	BLAST-DOMO
				affinis ¤2981229	

Table 3

Nucleotide SEQ ID NO:	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
67	434-478	Cardiovascular (0.238) Reproductive (0.238) Hematopoietic/Immune (0.190)	Cancer (0.429) Inflammation/Trauma (0.524) Cell Proliferation (0.095)	pINCY
68	380-424 551-595	Nervous (0.185) Reproductive (0.167) Gastrointestinal (0.148)	Cancer (0.444) Cell Proliferation (0.315) Inflammation/Trauma (0.278)	PINCY
69	433-477	Reproductive (0.429) Nervous (0.142) Hematopoietic/Immune (0.142)	Cancer (0.714) Inflammation/Trauma (0.142)	PINCY
70	684-728	Reproductive (0.333) Nervous (0.178) Cardiovascular (0.111)	Cancer (0.467) Cell Proliferation (0.244) Inflammation/Trauma (0.267)	PINCY
71	219-263	Hematopoietic/Immune (0.257) Reproductive (0.229) Gastrointestinal (0.143)	Cell Proliferation (0.400) Inflammation/Trauma (0.429) Cancer (0.314)	PINCY
72	865-912	Gastrointestinal (0.286) Reproductive (0.286) Cardiovascular (0.238)	Cancer (0.667) Cell Proliferation (0.143) Inflammation/Trauma (0.238)	PINCY
73	900-944	Reproductive (0.229) Hematopoietic/Immune (0.157) Nervous (0.157)	Cancer (0.422) Inflammation/Trauma (0.349) Cell Proliferation (0.205)	PINCY
74	109-153 919-963	Reproductive (0.270) Gastrointestinal (0.162) Cardiovascular (0.135)	Cancer (0.405) Cell Proliferation (0.270) Inflammation/Trauma (0.324)	pincy
75	1352-1396 1568-1612	Reproductive (0.296) Gastrointestinal (0.167) Nervous (0.167)	Cancer (0.509) Inflammation/Trauma (0.269) Cell Proliferation (0.157)	pINCY
76	541-585 1189-1233	Reproductive (0.238) Cardiovascular (0.190) Gastrointestinal (0.190)	Cancer (0.524) Inflammation/Trauma (0.310) Cell Proliferation (0.143)	PBLUESCRIPT
77	110-154	Reproductive (0.250) Nervous (0.224) Hematopoietic/Immune (0.132) Gastrointestinal (0.132)	Cancer (0.355) Inflammation/Trauma (0.342) Cell Proliferation (0.211)	PSPORT1
78	218-262	Reproductive (0.375) Nervous (0.188) Urologic (0.188)	Cancer (0.562) Inflammation/Trauma (0.250)	PINCY

WO 01/05970 PCT/US00/19698

		ליזווסס) כ סוחדו	110.)	
Nucleotide SEQ ID NO:	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
79	380-424	Hematopoietic/Immune (0.227) Nervous (0.227) Reproductive (0.227)	Inflammation/Trauma (0.636) Cancer (0.364)	PSPORT1
80	217-261	Reproductive (0.275) Gastrointestinal (0.196) Nervous (0.196)	Cancer (0.431) Inflammation/Trauma (0.451) Cell Proliferation (0.196)	PSPORT1
81	488-532 812-856	Reproductive (0.301) Nervous (0.151) Gastrointestinal (0.130)	Cancer (0.466) Inflammation/Trauma (0.288) Cell Proliferation (0.151)	pincy
82	595-639	Reproductive (0.333) Developmental (0.148) Gastrointestinal (0.148)	Cancer (0.444) Cell Proliferation (0.370) Inflammation/Trauma (0.333)	pINCY
83	219-263	Hematopoietic/Immune (0.400) Gastrointestinal (0.200) Cardiovascular (0.100)	Inflammation/Trauma (0.429) Cell Proliferation (0.357) Cancer (0.286)	PINCY
84	164-208	Cardiovascular (0.667) Nervous (0.222) Hematopoietic/Immune (0.111)	Cancer (0.556) Cell Proliferation (0.111)	PBLUESCRIPT
	487-531 757-801	Reproductive (0.182) Cardiovascular (0.091)	Cancer (0.308) Cell Proliferation (0.231) Inflammation/Trauma (0.154)	pINCY
98	325-369 811-855	Hematopoietic/Immune (0.288) Reproductive (0.197) Cardiovascular (0.136)	Inflammation (0.394) Cancer (0.318) Cell Proliferation (0.212)	pINCY
87	163-207	Reproductive (0.218) Nervous (0.172) Gastrointestinal (0.138)	Cancer (0.448) Cell Proliferation (0.218) Inflammation (0.207)	pincy
88 s	362-406 758-802	Reproductive (0.273) Gastrointestinal (0.227) Cardiovascular (0.136) Musculoskeletal (0.136)	Cancer (0.681) Cell Proliferation (0.182) Inflammation/Trauma (0.318)	pincy
89	272-316	Reproductive (0.229) Gastrointestinal (0.193) Nervous (0.193)	Cancer (0.404) Inflammation (0.220) Cell Proliferation (0.165)	pINCY

Nucleotide SEO ID NO:	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	V ctor
1	98-142	Nervous (0.400) Cardiovascular (0.200)	Cell Proliferation (0.400) Inflammation (0.400)	pINCY
		Developmental (0.200) Gastrointestinal (0.200)	Cancer (0.200)	
91	384-428 2016-2060	Reproductive (0.221) Gastrointestinal (0.156) Hematopojetic/Immune (0.143)	Cancer (0.468) Inflammation/Trauma (0.325) Cell Proliferation (0.273)	PBLUESCRIPT
92	80-124		Cancer (0.469) Inflammation/Trauma (0.326)	PBLUESCRIPT
			Cell Proliferation (0.306)	
63	437-481 641-685	Reproductive (0.250) Nervous (0.200)	Cancer (0.550) Inflammation/Trauma (0.284)	PBLUESCRIPT
		Cardiovascular (0.183)	Cell Proliferation (0.150)	
94	397-441 1036-1080	Reproductive (0.291) Hematopoietic/Immune (0.228) Nervous (0.152)	Inflammation/Trauma (0.468) Cancer (0.392) Cell Proliferation (0.165)	PINCY
95	247-291	Reproductive (0.242)	Cancer (0.455)	PINCY
		Hematopoietic/Immune (0.121)	Intlammation/Trauma (0.333)	
		Nervous (0:121) Urologic (0:121)	Cell Floilleideidi (C.2.)	
96	453-497 858-902	Nervous (0.600) Reproductive (0.400)	Cancer (0.400) Inflammation/Trauma (0.200) Neurological (0.200)	pINCY
0.7	236-166	Castrointestinal (0.060)	Cancor (0.462)	DINCY
	770-814	Reproductive (0.215)	Inflammation/Trauma (0.339)	4
000	5 47	Nervous (0.109)	Canon 10 5531	VONTO
886	3-4/ 1086-1130	keproductive (U.211) Gastrointestinal (U.211) Hematonoietic/Immune (U.158)	Calicer (0.353) Cell Proliferation (0.368) Inflammation/Trauma (0.342)	
66	388-432	oductive (0.268)	Cancer (0.390)	pINCY
	874-918	Nervous (0.146) Cardiovascular (0.146)	Inflammation/Trauma (0.390) Cell Proliferation (0.220)	
100	26-70	Gastrointestinal (0.238)		PINCY
		Cardiovascular (0.190)	Intlammation/Trauma (0.381)	
		Hemacopoletic/immune (0.143) Nervous (0.143)	Cell Froilieración (U.130)	
		Endocrine (0.143)		

Nucleotide SFO ID NO:	Selected	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
101	226-270	Nervous (0.234)	Inflammation/Trauma (0.383)	pINCY
	9017-7907	oductive (0.149)	Cell Proliferation (0.213)	
102	487-531	Reproductive (0.276)	Cancer (0.494)	PINCY
		Nervous (0.161)	cell Proliferation (0.310)	
		Gastrointestinal (0.138) Cardiovascular (0.138)	Inflammation/Trauma (0.264)	
103	561-605	Reproductive (0.274)	Cancer (0.452)	pINCY
		Gastrointestinal (0.194)	Inflammation/Trauma (0.339)	
	100	Cartaconiar (C. 127)	(0 800)	DINCY
104	287-331 806-850	Gastrointestinal (0.500) Reproductive (0.250) Musculoskeletal (0.250)	Inflammation/Trauma (0.250)	
105	154-198	Gastrointestinal (0.233)	Cancer (0.465)	PINCY
	505-549	Reproductive (0.209)	Inflammation/Trauma (0.326)	
	757-801	Hematopoietic/Immune (0.163) Nervous (0.163)	Cell Proliferation (0.209)	
106	174-218	Reproductive (0.185)	Inflammation/Trauma (0.352)	PINCY
	1182-1226	Hematopoietic/Immune (0.185) Nervous (0.185)	Cell Proliferation (0.333) Cancer (0.315)	
107	120-164	Reproductive (0.231)	Cell Proliferation (0.462)	PINCY
	489-533	Hematopoietic/Immune (0.231)	Inflammation/Trauma (0.385)	
		Nervous (0.154) Cardiovascular (0.154)	Cancer (0.231)	
108	64-108	ous (0.277)	Cancer (0.362)	PINCY
1	1738-1782	. 0	Inflammation/Trauma (0.362)	
		Cardiovascular (0.160)	Cell Proliferation (0.149)	
10963.	415-459	oductive (0.274)	Inflammation/Trauma (0.476)	PINCY
	1027-1071	Hematopoietic/Immune (0.226)	cancer (0.333) Cell Proliferation (0.179)	
110	242-286	Reproductive (0.500)	Cancer (1.000)	DINCY
		Nervous (0.500)		1000000
111	488-541	Reproductive (0.270)	Cancer (0.50/) Inflammation/Pranma (0.284)	FSFORTI
	1901-9701	Nervous (0.131) Gastrointestinal (0.126)	Cell Proliferation (0.172)	

WO 01/05970 PCT/US00/19698

	Vector	pincy	pincy	pINCY	pincy	PSPORT1	pincy	pincy	PSPORT1	pincy	pINCY	pINCY	******
116.)	Disease or Condition (Fraction of Total)	Cancer (0.469) Inflammation/Trauma (0.328) Cell Proliferation (0.172)	Cancer (0.445) Cell Proliferation (0.227) Inflammation/Trauma (0.327)	cancer (0.471) Inflammation/Trauma (0.118)	Cancer (0.476) Cell Proliferation (0.190) Inflammation/Trauma (0.238)	Cancer (0.600) Inflammation/Trauma (0.334) Cell Proliferation (0.067)	Cancer (0.531) Cell Proliferation (0.224) Inflammation/Trauma (0.265)	Cancer (0.446) Inflammation/Trauma (0.343) Cell Proliferation (0.226)	Cancer (0.517) Cell Proliferation (0.167) Inflammation/Trauma (0.235)	Cancer (0.429) Inflammation/Trauma (0.572) Cell Proliferation (0.143)	Cancer (0.340) Inflammation/Trauma (0.440) Cell Proliferation (0.200)	Cancer (0.680) Cell Proliferation (0.120) Inflammation/Trauma (0.160)	A
Table 2 (voite)	Tissue Expression (Fraction of Total)	12)	Reproductive (0.245) Gastrointestinal (0.136) Marvois (0.136)	Nervous (0.314) Rervous (0.314) Gastrointestinal (0.098)	Gastrointestinal (0.190) Nervous (0.190) Reproductive (0.190)	Reproductive (0.400) Nervous (0.267) Musculoskeletal (0.133)	Reproductive (0.327) Nervous (0.184) Hrologic (0.102)	Reproductive (0.231) Nervous (0.190) Gastrointestinal (0.169)	Reproductive (0.292) Nervous (0.163) Gastrointestinal (0.139)	Nervous (0.571) Cardiovascular (0.143) Developmental (0.143)	Nervous (0.300) Hematopoietic/Immune (0.200) Cardiovascular (0.140)	Reproductive (0.400) Cardiovascular (0.160) Nervous (0.160)	
	Selected	 	866-1135	155-325 812-1105	14-298	41-235	379-432 973-1026	974-1465	543-1028	385-552	685-864	703-1026	***
	Nucleotide	112	113	114	115	116	117	118	119	120	121	122	

	Selected Fragments	Tissue Expression (Fraction of Total)	Disease or Condition (Fraction of Total)	Vector
27.	272-325	Cardiovascular (0.250) Gastrointestinal (0.250) Musculoskeletal (0.250)	Inflammation/Trauma (0.750)	pincy
[-	130-972	Reproductive (0.180) Cardiovascular (0.160) Hematopoietic/Immune (0.160)	Cancer (0.440) Inflammation/Trauma (0.340) Cell Proliferation (0.220)	pincy
4	434-973	Reproductive (0.188) Cardiovascular (0.156) Gastrointestinal (0.156)	Cancer (0.422) Inflammation/Trauma (0.328) Cell Proliferation (0.203)	pincy
	489-899	Gastrointestinal (0.333) Reproductive (0.333) Nervous (0.125)	Cancer (0.625) Inflammation/Trauma (0.208) Cell Proliferation (0.042)	PINCY
	19-1242	Reproductive (0.354) Nervous (0.188) Gastrointestinal (0.146)	Cancer (0.562) Cell Proliferation (0.250) Inflammation/Trauma (0.250)	pincy
	217-270 541-594	Reproductive (0.364) Cardiovascular (0.182) Gastrointestinal (0.182)	Cancer (0.636) Inflammation/Trauma (0.364)	pINCY
	115-864	Gastrointestinal (0.250) Hematopoietic/Immune (0.208) Nervous (0.208)	Cancer (0.500) Inflammation/Trauma (0.292)	pINCY
	255-308	Reproductive (0.265) Nervous (0.169) Gastrointestinal (0.120)	Cancer (0.482) Cell Proliferation (0.349) Inflammation/Trauma (0.253)	pINCY
	23-541	Nervous (0.909) Endocrine (0.091)	Cancer (0.636) Cell Proliferation (0.091) Inflammation/Trauma (0.182)	pincy

SEQ ID	Library	Library Comment
73	SPLNNOT12	Library was constructed using RNA isolated from spleen tissue removed from a 65-year-old female. Pathology indicated the spleen was negative for metastasis. Pathology for the associated tumor tissue indicated well-differentiated neuroendocrine carcinoma (islet cell tumor), nuclear grade 1, forming a dominant mass in the distal pancreas. Multiple smaller tumor nodules were immediately adjacent to the main mass. The liver showed metastatic grade 1 islet cell tumor. forming multiple nodules. Multiple (4) pericholedochal lymph nodes contained metastatic grade 1 islet cell tumor.
74	MONOTXT02	om treated monocytes from periph were treated with interleukin-10 time 0 at 10 ng/ml, LPS was adde fy coat by adherence to plastic.
75	FIBPFENOG	vas constructed from 1.56 million independent clones from a prostate strissue library. Starting RNA was made from fibroblasts of prostate from a male fetus, who died after 26 weeks' gestation. The libraries we bunds using conditions adapted from Soares et al. (1994) Proc. Natl. A and Bonaldo et al. (1996) Genome Research 6:791, except that a significial reannealing hybridization was used.
76	HUVESTB01	Library was constructed using RNA isolated from shear-stressed HUV-EC-C (ATCC CRL 1/30) cells. Before RNA isolation, the cells were subjected to a shear stress of 10 dynes/cm.
77	SYNOOAT01	
78	UTRSNOT05	Library was constructed using RNA isolated from the uterine tissue of a 45-year-old Caucasian female during a total abdominal hysterectomy and total colectomy. Pathology for the associated tumor tissue indicated multiple leiomyomas of the myometrium and a grade 2 colonic adenocarcinoma of the cecum. Patient history included multiple sclerosis and mitral valve disorder. Family history included type I diabetes, cerebrovascular disease, atherosclerotic coronary artery disease, malignant skin neoplasm, hypertension, and malignant neoplasm of the colon.
79	HIPONON01	Library was constructed from 1.2° million independent clones from a hippocampus library. RNA was isolated from the hippocampus tissue of a 72-year-old Caucasian female who died from an intracranial bleed. Patient history included nose cancer, hypertension, and arthritis. The normalization and hybridization conditions were adapted from Soares et al. (1994) Proc. Natl. Acad. Sci. USA 91:9228.

SEO	Library	Library Comment
NO.:		
08	BRSTTUTO3	Library was constructed using RNA isolated from breast tumor tissue removed from a 58-year-old Caucasian female during a unilateral extended simple mastectomy. Pathology indicated multicentric invasive grade 4 lobular carcinoma. The mass was identified in the upper outer quadrant, and three separate nodules were found in the lower outer quadrant of the left breast. Patient history included skin cancer, rheumatic heart disease, osteoarthritis, and tuberculosis. Family history included cerebrovascular disease, coronary artery aneurysm, breast cancer, prostate cancer, atherosclerotic coronary artery disease, and type I diabetes.
81	SININOTO1	Library was constructed using RNA isolated from ileum tissue obtained from the small intestine of a 4-year-old Caucasian female, who died from a closed head injury. Patient history included jaundice. Previous surgeries included a double hernia repair.
82	SINTFETO3	Library was constructed using RNA isolated from small intestine tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation.
83	HNT3AZT01	Library was constructed using RNA isolated from the hNT2 cell line (derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor). Cells were treated for three days with 0.35 micromolar 5-aza-2'-deoxycytidine (AZ).
84	ENDANOT01	Library was constructed using RNA isolated from aortic endothelial cell tissue from an explanted heart removed from a male during a heart transplant.
85	LUNGTUTO8	constructed using RNA isolated an male during a right upper lok grade 3 adenocarcinoma. Patient ase, an acute myocardial infarct rysm, tobacco abuse, and cardiacre, stomach cancer, and lung carase, and an acute myocardial infase, and an acute myocardial inf
98	OVARTUTIO	structed using RNA isolated rear-old Caucasian female and repair of inguinal by of colonic origin, forming an adenocarcinoma of colonic cystic cervicitis. It is over the overy, colon cancincluded emphysema, myocal hypertension, and hyperlession.

Library Comment	Library was constructed using RNA isolated from breast tissue removed from a 36-year-old	neoplasm, depressive disorder, hyperlipidemia, and a chronic stomach ulcer. Family history included cardiovascular and cerebrovascular disease; hyperlipidemia; skin, breast, esophageal, bladder, and bone cancer; and Hoddkin's lymphoma.	Library was constructed using RNA isolated from uterine endometrium tissue removed from a 29-year-old Caucasian female during a vaginal hysterectomy and cystocele repair. Pathology indicated the endometrium was secretory, and the cervix showed mild chronic cervicitis with	focal squamous metaplasia. Pathology for the associated tumor tissue indicated intramural uterine leiomyoma. Patient history included hypothyroidism, pelvic floor relaxation, and haranleria Family history included herical hypothogical transfer and the parable of the family history included herical hypothogical transfer and the parable of the family history included herical hypothogical transfer and the parable of the parab	emia.	Library was constructed using RNA isolated from diseased right breast tissue removed from a	46-year-old Caucasian female during a unilateral extended simple mastectomy and open breast biopsy. Pathology indicated mildly proliferative fibrocyctic change including intraduction	duct ectasia, papilloma formation, and ductal hyperplasia. Pathology for the associated	tumor tissue indicated multifocal ductal carcinoma in situ, both comedo and non-comedo	Trees, increar grave & with extensive intraductal calcifications. Patient history included deficiency anemia, normal delivery, chronic sinusitis, extrinsic asthma, and kidnev	~~	Library was constructed using RNA isolated from diseased liver tissue removed from a 63-	year-old Caucasian female during a liver transplant.Patient history included primary biliary cirrhosis. Serology was positive for anti-mitochondrial antibody.	Library was constructed using RNA isolated from HUV-EC-C (ATCC CRL 1730) cells	constructed using RNA isolated from testicular tissue removed	liver disease. Patient history included cirrhos	as construc	id hemorrhage.	Library was constructed using RNA isolated from lung tissue removed from a Caucasian female fetus, who died at 20 weeks' gestation.	/ was
Library	BRSTNOT13	_	UTRSNOR01			BRSTTMT02						LIVRDIR01		HUVENOB01	TESTNOT03	:	LUNGNOT02		LUNGFET03	PANCNOT07
SEQ	NO:		88			8						90		91	92		93		94	95

		Table 4 (cont.)
SEQ TO NO:	Library	Library Comment
96	BRAINOT12	
26	LIVRTUT01	om liver tumor tissue removed ny. Pathology indicated metas amily history included a mal
86	GBLATUT01	Library was constructed using RNA isolated from gall bladder tumor tissue removed from a 78-year-old Caucasian female during a cholecystectomy. Pathology indicated invasive grade 2 squamous cell carcinoma, forming a mass in the gall bladder. Patient history includ d diverticulitis of the colon, palpitations, benign hypertension, and hyperlipidemia. Family history included a cholecystectomy, atherosclerotic coronary artery disease, hyperlipidemia, and benign hypertension.
66	LEUKNOT02	Library was constructed using RNA isolated from white blood cells of a 45-year-old female with blood type 0+. The donor tested positive for cytomegalovirus (CMV).
100	LUNGNOT22	Library was constructed using RNA isolated from lung tissue removed from a 58-year-old Caucasian female. The tissue sample used to construct this library was found to have tumor contaminant upon microscopic examination. Pathology for the associated tumor tissue indicated a caseating granuloma. Family history included congestive heart failure, br ast cancer, secondary bone cancer, acute myocardial infarction and atherosclerotic coronary artery disease.
101	ADRETUT06	from a indicat the adr
102	ADRETUT06	Library was constructed using RNA isolated from adrenal tumor tissue removed from a 57-year-old Caucasian female during a unilateral right adrenalectomy. Pathology indicated pheochromocytoma, forming a nodular mass completely replacing the medulla of the adrenal gland.
103	THYRNOT10	Library was constructed using RNA isolated from diseased left thyroid tissue removed from a 30-year-old Caucasian female during a unilateral thyroid lobectomy and parathyroid reimplantation. Pathology indicated lymphocytic thyroiditis.

SEQ ID NO:	Library	Library Comment
104	CONNTUTOS	Library was constructed using RNA isolated from tumorous skull soft tissue removed from a 34-year-old Caucasian female during skull lesion excision. Pathology indicated grade 3 ependymoma forming an implant in the dermis and subcutis associated with dense fibrosis. Patient history included seizures, bone cancer, and brain cancer. Surgeries included cranioplasty and cerebral meninges lesion excision, and treatment included whole brain radiation. Family history included anxiety and depression.
105	HEAANOT01	Library was constructed using RNA isolated from right coronary and right circumflex coronary artery tissue removed from the explanted heart of a 46-year-old Caucasian male during a heart transplantation. Patient history included myocardial infarction from total occlusion of the left anterior descending coronary artery, atherosclerotic coronary artery disease, hyperlipidemia, myocardial ischemia, dilated cardiomyopathy, left ventricular dysfunction, and tobacco abuse. Family history included atherosclerotic coronary artery disease.
106	UTRMTMT01	Library was constructed using RNA isolated from myometrial tissue removed from a 45-year-old Caucasian female during vaginal hysterectomy and bilateral salpingo-oophorectomy. Pathology indicated the myometrium was negative for tumor. Pathology for the associated tumor tissue indicated multiple (23) subserosal, intramural, and submucosal leiomyomata. The endometrium was in proliferative phase. The right ovary contained an old corpus luteum. The cervix, left overy, and right and left fallopian tubes were unremarkable. The patient presented with stress incontinence. Patient history included extrinsic asthma without status asthmaticus and normal delivery. Patient medications included Motrin, iron sulfate, Premarin, prednisone, Tylenol #3, and Colace. Family history included cerebrovascular disease, depression, and atherosclerotic coronary artery disease.
107	FIBPFEN06	This normalized library was constructed from 1.56 million independent clones from a prostate stromal fibroblast library. RNA was isolated from a male fetus, who died after 26 weeks' gestation. The normalization and hybridization conditions were adapted from Soares et al. (1994) Proc. Natl. Acad. Sci. USA 91:9228

I adde 4 (colle,)	Library Comment	Library was constructed using RNA isolated from pancreatic tumor tissue removed from a 45-year-old Caucasian female during radical pancreaticoduodenectomy. Pathology indicated a grade 4 anaplastic carcinoma. Family history included benign hypertension, hyperlipidemia and atherosclerotic coronary artery disease.	 	Library was frontal lob Pathology included be		Library was constructed using RNA from the explanted heart of a male	Library treated cells tr subtract polyA RI 1 cell million were bas Bonaldo	<pre>leukemla (ref: int. J. Cancer (1980) 26:1/1). 6 Library was constructed using RNA isolated from adrenal tumor tissue removed from a 57- year-old Caucasian female during a unilateral right adrenalectomy. Pathology indicated pheochromocytoma, forming a nodular mass completely replacing the medulla of the adrenal fland</pre>
	Library	PANCTUT02	LIVRFET02	BRAITUT03	BRSTNOT07	SMCANOT01	THP1AZS08	ADRETUT06
	SEQ ID NO:	114	115	116	117	118	119	120

SEQ ID NO:	Library	Library Comment
121	SININOTO3	Library was constructed using RNA isolated from ileum tissue obtained from an 8-year-old caucasian female, who died from head trauma. Serology was positive for cytomegalovirus (CMV).
122	SININOTO3	Library was constructed using RNA isolated from ileum tissue obtained from an 8-year-old caucasian female, who died from head trauma. Serology was positive for cytomegalovirus (CMV).
123	TLYMNOT06	Library was constructed using RNA isolated from activated Th2 cells. These cells were differentiated from umbilical cord CD4 T cells with IL-4 in the presence of anti-IL-12 antibodies and B7-transfected COS cells, and then activated for six hours with anti-CD3 and anti-CD28 antibodies.
124	HEAANOT01	and right circumflex 6-year-old Caucasian mal rdial infarction from to erosclerotic coronary ar opathy, left ventricular rdiac catheterization. F
125	TLYJ INTO1	Library was constructed using RNA isolated from a Jurkat cell line derived from the T cells of a male. The cells were treated for 18 hours with 50 ng/ml phorbol ester (PMA) and 1 micromolar calcium ionophore. Patient history included acute T-cell leukemia.
126	BRAITUT24	Library was constructed using RNA isolated from right frontal brain tumor tissue removed from a 50-year-old Caucasian male during a cerebral meninges lesion excision. Pathology indicated meningioma. Family history included colon cancer and cerebrovascular disease.
127	PROSTUT16	Library was constructed using RNA isolated from prostate tumor tissue removed from a 55-year-old Caucasian male. Pathology indicated adenocarcinoma, Gleason grade 5+4. Adenofibromatous hyperplasia was also present. The patient presented with elevated prostate specific antigen (PSA). Patient history included calculus of the kidney. Family history included lung cancer and breast cancer.
128	BRONNOT01	Library was constructed using RNA isolated from bronchial tissue removed from a 15-year-old Caucasian male.

Table 4 (cont.)

SEQ	Library	Library Comment
NO:		18- 18- From a time time to the 18-
129		BLADTUTU3 Library was constructed using RNA isolated from Diadder Lumbi Lissue temporational lymph year-old Caucasian male during a radical cystectomy, radical prostatectomy, regional lymph node excision, and urinary diversion to bowel. Pathology indicated invasive grade 3
130	COLXTDT01	r gion
		biopsy, and incidental appendectomy. Pathology indicated an unremarkable appendix.
		Pathology for the associated the premental menorrhagia and sarcoidosis of the lung. Family
		history included acute myocardial infarction and atherosclerotic coronary artery disease.
131	BRATNOT02	Library was constructed using RNA isolated from superior temporal cortex tissue removed
		from the prain of a 33-year of cardiomyopathy, congestive heart failure, and an enlarged spleen history included dilated cardiomyopathy, congestive heart failure, and an enlarged spleen
		and liver.
132	BRAWNOT01	Library was constructed using RNA isolated from dentate nucleus tissue removed from the
		brain of a 35-year-old Caucasian male who died flow catulated and the carehral necontex.
_		moderate leptomeningeal fibrosis and multiple microinfactors of any failure cardiomedaly.
		Patient history included dilated cardiomyopathy, congestive heart failure, curtismestry,
		and an enlarged spleen and liver.

Table 5 (cont.)

Program		Description	Reference	Parameter Threshold
ProfileScan	c	An algorithm that searches for structural and sequence motifs in protein sequences that match sequence patterns defined in Prosite.	Gribskov, M. et al. (1988) CABIOS 4:61-66; Gribskov, M. et al. (1989) Methods Enzymol. 183:146-159; Bairoch, A. et al. (1997) Nucleic Acids Res. 25:217-221.	Normalized quality score s GCG-specified "HIGH" value for that particular Prosite motif. Generally, score=1.4-2.1.
Phred	-	A base-calling algorithm that examines automated sequencer traces with high sensitivity and probability.	Ewing, B. et al. (1998) Genome Res. 8:175-185; Ewing, B. and P. Green (1998) Genome Res. 8:186-194.	
Phrap		A Phils Revised Assembly Program including SWAT and CrossMatch, programs based on efficient implementation of the Smith-Waterman algorithm, useful in searching sequence homology and assembling DNA sequences.	Smith, T.F. and M.S. Waterman (1981) Adv. Appl. Math. 2:482-489; Smith, T.F. and M.S. Waterman (1981) J. Mol. Biol. 147:195-197; and Green, P., University of Washington, Seattle, WA.	Score= 120 or greater; Match length= 56 or greater
Consed		A graphical tool for viewing and editing Phrap assemblies.	Gordon, D. et al. (1998) Genome Res. 8:195-202.	
SPScan		A weight matrix analysis program that scans protein sequences for the presence of secretory signal peptides.	Nielson, H. et al. (1997) Protein Engineering 10:1-6; Claverie, J.M. and S. Audic (1997) CABIOS 12:431-439.	Score=3.5 or greater
Motifs	2 ,2	A program that searches amino acid sequences for patterns that matched those defined in Prosite.	Bairoch, A. et al. (1997) Nucleic Acids Res. 25:217-221; Wisconsin Package Program Manual, version 9, page M51-59, Genetics Computer Group, Madison, WI.	

What is claimed is:

1. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

- a) an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61,
 15 SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, and SEQ ID NO:66,
- b) a naturally occurring amino acid sequence having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, and SEQ ID NO:66,
- c) a biologically active fragment of an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:52, SEQ ID NO:52, SEQ ID NO:55, SEQ ID NO:5

NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, and SEQ ID NO:66, and

- d) an immunogenic fragment of an amino acid sequence selected from the group consisting

 of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ

 ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID

 NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID

 NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID

 NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID

 NO:33, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID

 NO:40, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID

 NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:53, SEQ ID

 NO:54, SEQ ID NO:55, SEQ ID NO:66, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID

 NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, and SEQ

 ID NO:66.
- An isolated polypeptide of claim 1 selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66.
 - 3. An isolated polynucleotide encoding a polypeptide of claim 1.

- 4. An isolated polynucleotide encoding a polypeptide of claim 2.
- An isolated polynucleotide of claim 4 selected from the group consisting of SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID

NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, and SEQ ID NO:132.

- 6. A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 3.
 - 7. A cell transformed with a recombinant polynucleotide of claim 6.
- 8. A transgenic organism comprising a recombinant polynucleotide of claim 6.
 - 9. A method for producing a polypeptide of claim 1, the method comprising:
- a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said
 cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide
 comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim
 1, and
 - b) recovering the polypeptide so expressed.
 - 10. An isolated antibody which specifically binds to a polypeptide of claim 1.

- 11. An isolated polynucleotide comprising a polynucleotide sequence selected from the group consisting of:
- a) a polynucleotide sequence selected from the group consisting of SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106,
 35 SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:119,

SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, and SEQ ID NO:132,

- b) a naturally occurring polynucleotide sequence having at least 70% sequence identity to a
 5 polynucleotide sequence selected from the group consisting of SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, and SEQ ID NO:132,
 - c) a polynucleotide sequence complementary to a),
 - d) a polynucleotide sequence complementary to b), and
 - e) an RNA equivalent of a)-d).

- 12. An isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of claim 11.
- 13. A method for detecting a target polynucleotide in a sample, said target polynucleotide25 having a sequence of a polynucleotide of claim 11, the method comprising:
 - a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and
- b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.
 - 14. A method of claim 13, wherein the probe comprises at least 60 contiguous nucleotides.
- 15. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

- 16. A composition comprising an effective amount of a polypeptide of claim 1 and a pharmaceutically acceptable excipient.
- 17. A composition of claim 16, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126. SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:131, and SEQ ID NO:132.
- 18. A method for treating a disease or condition associated with decreased expression of functional GBAP, comprising administering to a patient in need of such treatment the pharmaceutical25 composition of claim 16.
 - 19. A method for screening a compound for effectiveness as an agonist of a polypeptide of claim 1, the method comprising:
 - a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
- b) detecting agonist activity in the sample.
 - 20. A composition comprising an agonist compound identified by a method of claim 19 and a pharmaceutically acceptable excipient.
- 21. A method for treating a disease or condition associated with decreased expression of functional GBAP, comprising administering to a patient in need of such treatment a pharmaceutical

composition of claim 20.

22. A method for screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, the method comprising:

- a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
- b) detecting antagonist activity in the sample.
- 23. A composition comprising an antagonist compound identified by a method of claim 22 and a pharmaceutically acceptable excipient.

10

- 24. A method for treating a disease or condition associated with overexpression of functional GBAP, comprising administering to a patient in need of such treatment a pharmaceutical composition of claim 23.
- 25. A method of screening for a compound that specifically binds to the polypeptide of claim 1, said method comprising the steps of:
 - a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and
- b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a 20 compound that specifically binds to the polypeptide of claim 1.
 - 26. A method of screening for a compound that modulates the activity of the polypeptide of claim 1, said method comprising:
- a) combining the polypeptide of claim 1 with at least one test compound under conditions
 25 permissive for the activity of the polypeptide of claim 1,
 - b) assessing the activity of the polypeptide of claim 1 in the presence of the test compound, and
- c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change
 30 in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.
- 27. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method35 comprising:
 - a) exposing a sample comprising the target polynucleotide to a compound, and

- b) detecting altered expression of the target polynucleotide.
- 28. A method for assessing toxicity of a test compound, said method comprising:
- a) treating a biological sample containing nucleic acids with the test compound;
- b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 11 or fragment thereof;
- 10 c) quantifying the amount of hybridization complex; and
 - d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

SEQUENCE LISTING

```
<110> INCYTE GENOMICS, INC.
      YUE, Henry
      TANG, Y. Tom
      BANDMAN, Olga
      HILLMAN, Jennifer L.
      LAL, Preeti
      AU-YOUNG, Janice
      REDDY, Roopa
      YANG, Junming
      BAUGHN, Mariah R.
      LU, Dyung Aina M.
      AZIMZAI, Yalda
      PATTERSON, Chandra
<120> GTP-BINDING ASSOCIATED PROTEINS
<130> PF-0714 PCT
<140> To Be Assigned
<141> Herewith
<150> 60/144,595; 60/150,460; 60/159,849
<151> 1999-07-19; 1999-08-23; 1999-10-15
<160> 132
<170> PERL Program
<210> 1
<211> 269
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1405545CD1
<400> 1
Met Pro Ala Val Leu Glu Arg Leu Ser Arg Tyr Asn Ser Thr Ser
  1
                                     10
Gln Ala Phe Ala Glu Val Leu Arg Leu Pro Lys Gln Gln Leu Arg
                 20
                                     25
Lys Leu Leu Tyr Pro Leu Gln Glu Val Glu Arg Phe Leu Ala Pro
                                     40
                 35
Tyr Gly Arg Gln Asp Leu His Leu Arg Ile Phe Asp Pro Ser Pro
                 50
                                     55
                                                          60
Glu Asp Ile Ala Arg Ala Asp Asn Ile Phe Thr Ala Thr Glu Arg
                 65
Asn Arg Ile Asp Tyr Val Ser Ser Ala Val Arg Ile Asp His Ala
                                     85 ·
                 80
Pro Asp Leu Pro Arg Pro Glu Val Cys Phe Ile Gly Arg Ser Asn
                 95
                                    100
Val Gly Lys Ser Ser Leu Ile Lys Ala Leu Phe Ser Leu Ala Pro
                110
                                    115
                                                         120
Glu Val Glu Val Arg Val Ser Lys Lys Pro Gly His Thr Lys Lys
                125
                                    130
                                                         135
Met Asn Phe Phe Lys Val Gly Lys His Phe Thr Val Val Asp Met
                140
                                    145
                                                         150
Pro Gly Tyr Gly Phe Arg Ala Pro Glu Asp Phe Val Asp Met Val
                155
                                    160
Glu Thr Tyr Leu Lys Glu Arg Arg Asn Leu Lys Arg Thr Phe Leu
```

```
175
Leu Val Asp Ser Val Val Gly Ile Gln Lys Thr Asp Asn Ile Ala
                                    190
                185
Ile Glu Met Cys Glu Glu Phe Ala Leu Pro Tyr Val Ile Val Leu
                                    205
                200
                                                         210
Thr Lys Ile Asp Lys Ser Ser Lys Gly His Leu Leu Lys Gln Val
                                    220
                215
Leu Gln Ile Gln Lys Phe Val Asn Met Lys Thr Gln Gly Cys Phe
                230
                                    235
Pro Gln Leu Phe Pro Val Ser Ala Val Thr Phe Ser Gly Ile His
                                    250
                245
Leu Leu Arg Cys Phe Ile Ala Ser Val Thr Gly Ser Leu Asp
                260
                                    265
<210> 2
<211> 428
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1451265CD1
<400> 2
Met Glu Val Ala Val Cys Thr Asp Ser Ala Ala Pro Met Trp Ser
                                     10
Cys Ile Val Trp Glu Leu His Ser Gly Ala Asn Leu Leu Thr Tyr
                 20
Arg Gly Gly Gln Ala Gly Pro Arg Gly Leu Ala Leu Leu Asn Gly
                 35
                                     40
Glu Tyr Leu Leu Ala Ala Gln Leu Gly Lys Asn Tyr Ile Ser Ala
                 50
                                     55
Trp Glu Leu Gln Arg Lys Asp Gln Leu Gln Gln Lys Ile Met Cys
                 65
                                     70
Pro Gly Pro Val Thr Cys Leu Thr Ala Ser Pro Asn Gly Leu Tyr
                 80
                                     85
Val Leu Ala Gly Val Ala Glu Ser Ile His Leu Trp Glu Val Ser
                 95
                                    100
                                                         105
Thr Gly Asn Leu Leu Val Ile Leu Ser Arg His Tyr Gln Asp Val
                110
                                    115
                                                         120
Ser Cys Leu Gln Phe Thr Gly Asp Ser Ser His Phe Ile Ser Gly
                125
                                    130
                                                         135
Gly Lys Asp Cys Leu Val Leu Val Trp Ser Leu Cys Ser Val Leu
                140
                                    145
                                                         150
Gln Ala Asp Pro Ser Arg Ile Pro Ala Pro Arg His Val Trp Ser
                155
                                    160
                                                         165
His His Thr Leu Pro Ile Thr Asp Leu His Cys Gly Phe Gly Gly
                170
                                    175
                                                         180
Pro Leu Ala Arg Val Ala Thr Ser Ser Leu Asp Gln Thr Val Lys
                185
                                    190
                                                         195
Leu Trp Glu Val Ser Ser Gly Glu Leu Leu Ser Val Leu Phe
                200
                                    205
                                                         210
Asp Val Ser Ile Met Ala Val Thr Met Asp Leu Ala Glu His His
                215
                                    220
                                                         225
Met Phe Cys Gly Gly Ser Glu Gly Ser Ile Phe Gln Val Asp Leu
                230
                                    235
Phe Thr Trp Pro Gly Gln Arg Glu Arg Ser Phe His Pro Glu Gln
                245
                                    250
                                                         255
Asp Ala Gly Lys Val Phe Lys Gly His Arg Asn Gln Val Thr Cys
                260
                                    265
                                                         270
Leu Ser Val Ser Thr Asp Gly Ser Val Leu Leu Ser Gly Ser His
                                    280
                275
                                                         285
Asp Glu Thr Val Arg Leu Trp Asp Val Gln Ser Lys Gln Cys Ile
                290
                                    295
```

```
Arg Thr Val Ala Leu Lys Gly Pro Val Thr Asn Ala Ala Ile Leu
                                     310
Leu Ala Pro Val Ser Met Leu Ser Ser Asp Phe Arg Pro Ser Leu
                                     325
                320
                                                         330
Pro Leu Pro His Phe Asn Lys His Leu Leu Gly Ala Glu His Gly
                335
                                     340
Asp Glu Pro Arg His Gly Gly Leu Thr Leu Arg Leu Gly Leu His
                350
                                    355
                                                         360
Gln Gln Gly Ser Glu Pro Ser Tyr Leu Asp Arg Thr Glu Gln Leu
                                     370
                                                         375
                365
Gln Ala Val Leu Cys Ser Thr Met Glu Lys Ser Val Leu Gly Gly
                                     385
                                                         390
                380
Gln Asp Gln Leu Arg Val Arg Val Thr Glu Leu Glu Asp Glu Val
                                     400
                                                         405
                395
Arg Asn Leu Arg Lys Ile Asn Arg Asp Leu Phe Asp Phe Ser Thr
                410
Arg Phe Ile Thr Arg Pro Ala Lys
                425
<210> 3
<211> 562
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1556311CD1
<400> 3
Met Pro Glu Thr Val Asn His Asn Lys His Gly Asn Val Ala Leu
                  5
                                      10
Pro Gly Thr Lys Pro Thr Pro Ile Pro Pro Pro Arg Leu Lys Lys
                 20
Gln Ala Ser Phe Leu Glu Ala Glu Gly Gly Ala Lys Thr Leu Ser
                 35
                                      40
Gly Gly Arg Pro Gly Ala Gly Pro Glu Leu Glu Leu Gly Thr Ala
                 50
                                     55
                                                          60
Gly Ser Pro Gly Gly Ala Pro Pro Glu Ala Ala Pro Gly Asp Cys
                 65
                                      70
Thr Arg Ala Pro Pro Pro Ser Ser Glu Ser Arg Pro Pro Cys His
                                                          90
                                     85
                 80
Gly Gly Arg Gln Arg Leu Ser Asp Met Ser Ile Ser Thr Ser Ser
                                    100
                                                         105
                 95
Ser Asp Ser Leu Glu Phe Asp Arg Ser Met Pro Leu Phe Gly Tyr
                110
                                     115
                                                         120
Glu Ala Asp Thr Asn Ser Ser Leu Glu Asp Tyr Glu Gly Glu Ser
                                    130
                125
Asp Gln Glu Thr Met Ala Pro Pro Ile Lys Ser Lys Lys Arg
                140
                                    145
                                                         150
Ser Ser Ser Phe Val Leu Pro Lys Leu Val Lys Ser Gln Leu Gln
                155
                                    160
Lys Val Ser Gly Val Phe Ser Ser Phe Met Thr Pro Glu Lys Arg
                170
                                    175
Met Val Arg Arg Ile Ala Glu Leu Ser Arg Asp Lys Cys Thr Tyr
                185
                                    190
Phe Gly Cys Leu Val Gln Asp Tyr Val Ser Phe Leu Gln Glu Asn
                200
                                    205
                                                         210
Lys Glu Cys His Val Ser Ser Thr Asp Met Leu Gln Thr Ile Arg
                215
                                    220
                                                         225
Gln Phe Met Thr Gln Val Lys Asn Tyr Leu Ser Gln Ser Ser Glu
                230
                                    235
Leu Asp Pro Pro Ile Glu Ser Leu Ile Pro Glu Asp Gln Ile Asp
                245
                                    250
Val Val Leu Glu Lys Ala Met His Lys Cys Ile Leu Lys Pro Leu
```

```
260
Lys Gly His Val Glu Ala Met Leu Lys Asp Phe His Met Ala Asp
                                    280
                275
Gly Ser Trp Lys Gln Leu Lys Glu Asn Leu Gln Leu Val Arg Gln
                290
                                     295
                                                         300
Arg Asn Pro Gln Glu Leu Gly Val Phe Ala Pro Thr Pro Asp Phe
                305
                                    310
                                                         315
Val Asp Val Glu Lys Ile Lys Val Lys Phe Met Thr Met Gln Lys
                320
                                    325
                                                         330
Met Tyr Ser Pro Glu Lys Lys Val Met Leu Leu Arg Val Cys
                335
                                    340
                                                         345
Lys Leu Ile Tyr Thr Val Met Glu Asn Asn Ser Gly Arg Met Tyr
                350
                                    355
                                                         360
Gly Ala Asp Asp Phe Leu Pro Val Leu Thr Tyr Val Ile Ala Gln
                365
                                     370
Cys Asp Met Leu Glu Leu Asp Thr Glu Ile Glu Tyr Met Met Glu
                380
                                    385
                                                         390
Leu Leu Asp Pro Ser Leu Leu His Gly Glu Gly Gly Tyr Tyr Leu
                395
                                     400
                                                         405
Thr Ser Ala Tyr Gly Ala Leu Ser Leu Ile Lys Asn Phe Gln Glu
                410
                                    415
                                                         420
Glu Gln Ala Ala Arg Leu Leu Ser Ser Glu Thr Arg Asp Thr Leu
                425
                                    430
                                                         435
Arg Gln Trp His Lys Arg Arg Thr Thr Asn Arg Thr Ile Pro Ser
                440
                                    445
                                                         450
Val Asp Asp Phe Gln Asn Tyr Leu Arg Val Ala Phe Gln Glu Val
                455
                                    460
                                                         465
Asn Ser Gly Cys Thr Gly Lys Thr Leu Leu Val Arg Pro Tyr Ile
                470
                                    475
Thr Thr Glu Asp Val Cys Gln Ile Cys Ala Glu Lys Phe Lys Val
                485
                                    490
                                                         495
Gly Asp Pro Glu Glu Tyr Ser Leu Phe Leu Phe Val Asp Glu Thr
                500
                                    505
                                                         510
Trp Gln Gln Leu Ala Glu Asp Thr Tyr Pro Gln Lys Ile Lys Ala
                515
                                    520
                                                         525
Glu Leu His Ser Arg Pro Gln Pro His Ile Phe His Phe Val Tyr
                530
                                    535
                                                         540
Lys Arg Ile Lys Asn Asp Pro Tyr Gly Ile Ile Phe Gln Asn Gly
                545
Glu Glu Asp Leu Thr Thr Ser
                560
<210> 4
<211> 229
<212> PRT
<213> Homo sapiens
<221> misc_feature
<223> Incyte ID No: 1901373CD1
<400> 4
Met Ala Glu Asp Lys Thr Lys Pro Ser Glu Leu Asp Gln Gly Lys
 1
                                     10
Tyr Asp Ala Asp Asp Asn Val Lys Ile Ile Cys Leu Gly Asp Ser
                 20
                                     25
Ala Val Gly Lys Ser Lys Leu Met Glu Arg Phe Leu Met Asp Gly
                 35
                                     40
                                                        45
Phe Gln Pro Gln Gln Leu Ser Thr Tyr Ala Leu Thr Leu Tyr Lys
                 50
                                     55
His Thr Ala Thr Val Asp Gly Arg Thr Ile Leu Val Asp Phe Trp
                 65
                                     70
Asp Thr Ala Gly Gln Glu Arg Phe Gln Ser Met His Ala Ser Tyr
                                     85
```

```
Tyr His Lys Ala His Ala Cys Ile Met Val Phe Asp Val Gln Arg
                                    100
                 95
Lys Val Thr Tyr Arg Asn Leu Ser Thr Trp Tyr Thr Glu Leu Arg
                110
                                    115
                                                         120
Glu Phe Arg Pro Glu Ile Pro Cys Ile Val Val Ala Asn Lys Ile
                125
                                    130
                                                         135
Asp Ala Asp Ile Asn Val Thr Gln Lys Ser Phe Asn Phe Ala Lys
                                    145
                                                         150
                140
Lys Phe Ser Leu Pro Leu Tyr Phe Val Ser Ala Ala Asp Gly Thr
                155
                                    160
                                                         165
Asn Val Val Lys Leu Phe Asn Asp Ala Ile Arg Leu Ala Val Ser
                170
                                    175
                                                         180
Tyr Lys Gln Asn Ser Gln Asp Phe Met Asp Glu Ile Phe Gln Glu
                185
                                    190
                                                         195
Leu Glu Asn Phe Ser Leu Glu Glu Glu Glu Asp Val Pro Asp
                200
                                    205
                                                         210
Gln Glu Gln Ser Ser Ile Glu Thr Pro Ser Glu Glu Val Ala
                215
                                    220
Ser Pro His Ser
<210> 5
<211> 360
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2367767CD1
<400> 5
Met Phe Val Ala Arg Ser Ile Ala Ala Asp His Lys Asp Leu Ile
                                     10
                                                          15
His Asp Val Ser Phe Asp Phe His Gly Arg Arg Met Ala Thr Cys
                 20
                                     25
Ser Ser Asp Gln Ser Val Lys Val Trp Asp Lys Ser Glu Ser Gly
                                     40
                 35
Asp Trp His Cys Thr Ala Ser Trp Lys Thr His Ser Gly Ser Val
                 50
                                     55
Trp Arg Val Thr Trp Ala His Pro Glu Phe Gly Gln Val Leu Ala
                 65
                                     70
Ser Cys Ser Phe Asp Arg Thr Ala Ala Val Trp Glu Glu Ile Val
                 80
                                     85
                                                         90
Gly Glu Ser Asn Asp Lys Leu Arg Gly Gln Ser His Trp Val Lys
                                    100
                                                         105
                 95
Arg Thr Thr Leu Val Asp Ser Arg Thr Ser Val Thr Asp Val Lys
                                    115
                110
                                                         120
Phe Ala Pro Lys His Met Gly Leu Met Leu Ala Thr Cys Ser Ala
                                    130
                                                        135
                125
Asp Gly Ile Val Arg Ile Tyr Glu Ala Pro Asp Val Met Asn Leu
                140
                                    145
                                                         150
Ser Gln Trp Ser Leu Gln His Glu Ile Ser Cys Lys Leu Ser Cys
                155
                                    160
Ser Cys Ile Ser Trp Asn Pro Ser Ser Arg Ala His Ser Pro
                170
                                    175
Met Ile Ala Val Gly Ser Asp Asp Ser Ser Pro Asn Ala Met Ala
                185
                                    190
Lys Val Gln Ile Phe Glu Tyr Asn Glu Asn Thr Arg Lys Tyr Ala
                200
                                    205
                                                        210
Lys Ala Glu Thr Leu Met Thr Val Thr Asp Pro Val His Asp Ile
                215
                                    220
                                                        225
Ala Phe Ala Pro Asn Leu Gly Arg Ser Phe His Ile Leu Ala Ile
                                    235
Ala Thr Lys Asp Val Arg Ile Phe Thr Leu Lys Pro Val Arg Lys
```

```
250
Glu Leu Thr Ser Ser Gly Gly Pro Thr Lys Phe Glu Ile His Ile
                260
                                    265
Val Ala Gln Phe Asp Asn His Asn Ser Gln Val Trp Arg Val Ser
                                    280
                                                         285
                275
Trp Asn Ile Thr Gly Thr Val Leu Ala Ser Ser Gly Asp Asp Gly
                290
                                     295
                                                         300
Cys Val Arg Leu Trp Lys Ala Asn Tyr Met Asp Asn Trp Lys Cys
                                                         315
                305
                                    310
Thr Gly Ile Leu Lys Gly Asn Gly Ser Pro Val Asn Gly Ser Ser
                320
                                                         330
                                    325
Gln Gln Gly Thr Ser Asn Pro Ser Leu Gly Ser Asn Ile Pro Ser
                                    340
                335
Leu Gln Asn Ser Leu Asn Gly Ser Ser Ala Gly Arg Lys His Ser
                350
                                    355
<210> 6
<211> 460
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3090433CD1
<400> 6
Met Ala Asn Asp Pro Leu Glu Gly Phe His Glu Val Asn Leu Ala
                  5
                                     10
Ser Pro Thr Ser Pro Asp Leu Leu Gly Val Tyr Glu Ser Gly Thr
                 20
                                     25
Gln Glu Gln Thr Thr Ser Pro Ser Val Ile Tyr Arg Pro His Pro
                                      40
                 35
Ser Ala Leu Ser Ser Val Pro Ile Gln Ala Asn Ala Leu Asp Val
                 50
                                     55
Ser Glu Leu Pro Thr Gln Pro Val Tyr Ser Ser Pro Arg Arg Leu
                 65
                                     70
Asn Cys Ala Glu Ile Ser Ser Ile Ser Phe His Val Thr Asp Pro
                 80
Ala Pro Cys Ser Thr Ser Gly Val Thr Ala Gly Leu Thr Lys Leu
                                    100
                 95
Thr Thr Arg Lys Asp Asn Tyr Asn Ala Glu Arg Glu Phe Leu Gln
                                    115
                110
                                                         120
Gly Ala Thr Ile Thr Glu Ala Cys Asp Gly Ser Asp Asp Ile Phe
                                    130
                125
Gly Leu Ser Thr Asp Ser Leu Ser Arg Leu Arg Ser Pro Ser Val
                140
                                    145
                                                         150
Leu Glu Val Arg Glu Lys Gly Tyr Glu Arg Leu Lys Glu Glu Leu
                155
                                    160
Ala Lys Ala Gln Arg Glu Leu Lys Leu Lys Asp Glu Glu Cys Glu
                170
                                    175
Arg Leu Ser Lys Val Arg Asp Gln Leu Gly Gln Glu Leu Glu Glu
                                    190
                185
Leu Thr Ala Ser Leu Phe Glu Glu Ala His Lys Met Val Arg Glu
                200
                                    205
                                                         210
Ala Asn Ile Lys Gln Ala Thr Ala Glu Lys Gln Leu Lys Glu Ala
                215
                                                         225
                                    220
Gln Gly Lys Ile Asp Val Leu Gln Ala Glu Val Ala Ala Leu Lys
                230
                                    235
                                                         240
Thr Leu Val Leu Ser Ser Ser Pro Thr Ser Pro Thr Gln Glu Pro
                245
                                    250
Leu Pro Gly Gly Lys Thr Pro Phe Lys Lys Gly His Thr Arg Asn
                260
                                    265
Lys Ser Thr Ser Ser Ala Met Ser Gly Ser His Gln Asp Leu Ser
```

```
275
                                    280
Val Ile Gln Pro Ile Val Lys Asp Cys Lys Glu Ala Asp Leu Ser
                290
                                    295
                                                         300
Leu Tyr Asn Glu Phe Arg Leu Trp Lys Asp Glu Pro Thr Met Asp
                                     310
                305
Arg Thr Cys Pro Phe Leu Asp Lys Ile Tyr Gln Glu Asp Ile Phe
                320
                                    325
Pro Cys Leu Thr Phe Ser Lys Ser Glu Leu Ala Ser Ala Val Leu
                                     340
                335
Glu Ala Val Glu Asn Asn Thr Leu Ser Ile Glu Pro Val Gly Leu
                350
                                     355
                                                         360
Gln Pro Ile Arg Phe Val Lys Ala Ser Ala Val Glu Cys Gly Gly
                365
                                     370
                                                         375
Pro Lys Lys Cys Ala Leu Thr Gly Gln Ser Lys Ser Cys Lys His
                                     385
                380
Arg Ile Lys Leu Gly Asp Ser Ser Asn Tyr Tyr Tyr Ile Ser Pro
                395
                                                         405
                                     400
Phe Cys Arg Tyr Arg Ile Thr Ser Val Cys Asn Phe Phe Thr Tyr
                410
                                     415
                                                         420
Ile Arg Tyr Ile Gln Gln Gly Leu Val Lys Gln Gln Asp Val Asp
                425
                                    430
                                                         435
Gln Met Phe Trp Glu Val Met Gln Leu Arg Lys Glu Met Ser Leu
                440
                                    445
Ala Lys Leu Gly Tyr Phe Lys Glu Glu Leu
                455
<210> 7
<211> 239
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3800591CD1
<400> 7
Met Gln Asp Pro Asn Ala Asp Thr Glu Trp Asn Asp Ile Leu Arg
                                     10
Lys Lys Gly Ile Leu Pro Pro Lys Glu Ser Leu Lys Glu Leu Glu
                 20
                                     25
Glu Glu Ala Glu Glu Gln Arg Ile Leu Gln Gln Ser Val Val
                 35
                                     40
Lys Thr Tyr Glu Asp Met Thr Leu Glu Glu Leu Glu Asp His Glu
                 50
                                     55
                                                          60
Asp Glu Phe Asn Glu Glu Asp Glu Arg Ala Ile Glu Met Tyr Arg
                                     70
                 65
Arg Arg Arg Leu Ala Glu Trp Lys Ala Thr Lys Leu Lys Asn Lys
                 80
                                     85
                                                          90
Phe Gly Glu Val Leu Glu Ile Ser Gly Lys Asp Tyr Val Gln Glu
                                    100
                                                         105
Val Thr Lys Ala Gly Glu Gly Leu Trp Val Ile Leu His Leu Tyr
                                                         120
                110
                                    115
Lys Gln Gly Ile Pro Leu Cys Ala Leu Ile Asn Gln His Leu Ser
                125
                                    130
Gly Leu Ala Arg Lys Phe Pro Asp Val Lys Phe Ile Lys Ala Ile
                140
                                    145
                                                         150
Ser Thr Thr Cys Ile Pro Asn Tyr Pro Asp Arg Asn Leu Pro Thr
                155
                                    160
                                                         165
Ile Phe Val Tyr Leu Glu Gly Asp Ile Lys Ala Gln Phe Ile Gly
                170
                                    175
                                                         180
Pro Leu Val Phe Gly Gly Met Asn Leu Thr Arg Asp Glu Leu Glu
                185
                                    190
                                                         195
Trp Lys Leu Ser Glu Ser Gly Ala Ile Met Thr Asp Leu Glu Glu
                200
```

```
Asn Pro Lys Lys Pro Ile Glu Asp Val Leu Leu Ser Ser Val Arg
                                    220
                215
Arg Ser Val Leu Met Lys Arg Asp Ser Asp Ser Glu Gly Asp
                230
<210> 8
<211> 334
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5308471CD1
Met Arg Leu Thr Pro Arg Ala Leu Cys Ser Ala Ala Gln Ala Ala
 1
Trp Arg Glu Asn Phe Pro Leu Cys Gly Arg Asp Val Ala Arg Trp
                 20
                                     25
Phe Pro Gly His Met Ala Lys Gly Leu Lys Lys Met Gln Ser Ser
                 35
                                      40
Leu Lys Leu Val Asp Cys Ile Ile Glu Val His Asp Ala Arg Ile
                 50
                                     55
Pro Leu Ser Gly Arg Asn Pro Leu Phe Gln Glu Thr Leu Gly Leu
                 65
                                     70
Lys Pro His Leu Leu Val Leu Asn Lys Met Asp Leu Ala Asp Leu
                 80
                                     85
Thr Glu Gln Gln Lys Ile Met Gln His Leu Glu Gly Glu Gly Leu
                 95
                                    100
Lys Asn Val Ile Phe Thr Asn Cys Val Lys Asp Glu Asn Val Lys
                                    115
                                                         120
                110
Gln Ile Ile Pro Met Val Thr Glu Leu Ile Gly Arg Ser His Arg
                125
                                    130
                                                         135
Tyr His Arg Lys Glu Asn Leu Glu Tyr Cys Ile Met Val Ile Gly
                140
                                    145
Val Pro Asn Val Gly Lys Ser Ser Leu Ile Asn Ser Leu Arg Arg
                                                         165
                155
                                    160
Gln His Leu Arg Lys Gly Lys Ala Thr Arg Val Gly Gly Glu Pro
                170
                                    175
Gly Ile Thr Arg Ala Val Met Ser Lys Ile Gln Val Ser Glu Arg
                185
                                    190
Pro Leu Met Phe Leu Leu Asp Thr Pro Gly Val Leu Ala Pro Arg
                200
                                    205
                                                         210
Ile Glu Ser Val Glu Thr Gly Leu Lys Leu Ala Leu Cys Gly Thr
                                    220
                215
                                                         225
Val Leu Asp His Leu Val Gly Glu Glu Thr Met Ala Asp Tyr Leu
                230
                                    235
Leu Tyr Thr Leu Asn Lys His Gln Arg Phe Gly Tyr Val Gln His
                                    250
                245
Tyr Gly Leu Gly Ser Ala Cys Asp Asn Val Glu Arg Val Leu Lys
                260
                                    265
                                                         270
Ser Val Ala Val Lys Leu Gly Lys Thr Gln Lys Val Lys Val Leu
                275
                                    280
Thr Gly Thr Gly Asn Val Asn Val Ile Gln Pro Asn Tyr Pro Ala
                290
                                    295
Ala Ala Arg Asp Phe Leu Gln Thr Phe Arg Arg Gly Leu Leu Gly
                305
                                    310
                                                         315
Ser Val Met Leu Asp Leu Asp Val Leu Arg Gly His Pro Pro Ala
                                                         330
                320
                                    325
Glu Thr Leu Pro
<210> 9
<211> 341
<212> PRT
```

```
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5324322CD1
<400> 9
Met Glu Arg Ala Val Pro Leu Ala Val Pro Leu Gly Gln Thr Glu
                                     10
Val Phe Gln Ala Leu Gln Arg Leu His Met Thr Ile Phe Ser Gln
Ser Val Ser Pro Cys Gly Lys Phe Leu Ala Ala Gly Asn Asn Tyr
                 35
                                     40
Gly Gln Ile Ala Ile Phe Ser Leu Ser Ser Ala Leu Ser Ser Glu
                                     55
Ala Lys Glu Glu Ser Lys Lys Pro Val Val Thr Phe Gln Ala His
                                     70
                 65
Asp Gly Pro Val Tyr Ser Met Val Ser Thr Asp Arg His Leu Leu
                                     85
                 80
Ser Ala Gly Asp Gly Glu Val Lys Ala Trp Leu Trp Ala Glu Met
                 95
                                    100
Leu Lys Lys Gly Cys Lys Glu Leu Trp Arg Arg Gln Pro Pro Tyr
                110
                                    115
                                                        120
Arg Thr Ser Leu Glu Val Pro Glu Ile Asn Ala Leu Leu Leu Val
                125
                                    130
Pro Lys Glu Asn Ser Leu Ile Leu Ala Gly Gly Asp Cys Gln Leu
                                    145
                140
His Thr Met Asp Leu Glu Thr Gly Thr Phe Thr Arg Val Leu Arg
                155
                                    160
Gly His Thr Asp Tyr Ile His Cys Leu Ala Leu Arg Glu Arg Ser
                170
                                    175
Pro Glu Val Leu Ser Gly Gly Glu Asp Gly Ala Val Arg Leu Trp
               185
                                    190
Asp Leu Arg Thr Ala Lys Glu Val Gln Thr Ile Glu Val Tyr Lys
                200
                                    205
                                                        210
His Glu Glu Cys Ser Arg Pro His Asn Gly Arg Trp Ile Gly Cys
                215
                                    220
Leu Ala Thr Asp Ser Asp Trp Met Val Cys Gly Gly Pro Ala
                230
                                    235
Leu Thr Leu Trp His Leu Arg Ser Ser Thr Pro Thr Thr Ile Phe
                                    250
                245
Pro Ile Arg Ala Pro Gln Lys His Val Thr Phe Tyr Gln Asp Leu
                260
                                    265
Ile Leu Ser Ala Gly Gln Gly Arg Cys Val Asn Gln Trp Gln Leu
                275
                                    280
Ser Gly Glu Leu Lys Ala Gln Val Pro Gly Ser Ser Pro Gly Leu
                290
                                    295
Leu Ser Leu Ser Leu Asn Gln Gln Pro Ala Ala Pro Glu Cys Lys
                                    310
                                                        315
Val Leu Thr Ala Ala Gly Asn Ser Cys Arg Val Asp Val Phe Thr
                320
                                    325
Asn Leu Gly Tyr Arg Ala Phe Ser Leu Ser Phe
                335
<210> 10
<211> 513
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 067184CD1
<400> 10
```

Met Ser Ile Glu Ile Glu Ser Ser Asp Val Ile Arg Leu Ile Met Gln Tyr Leu Lys Glu Asn Ser Leu His Arg Ala Leu Ala Thr Leu Gln Glu Glu Thr Thr Val Ser Leu Asn Thr Val Asp Ser Ile Glu Ser Phe Val Ala Asp Ile Asn Ser Gly His Trp Asp Thr Val Leu Gln Ala Ile Gln Ser Leu Lys Leu Pro Asp Lys Thr Leu Ile Asp Leu Tyr Glu Gln Val Val Leu Glu Leu Ile Glu Leu Arg Glu Leu Gly Ala Ala Arg Ser Leu Leu Arg Gln Thr Asp Pro Met Ile Met Leu Lys Gln Thr Gln Pro Glu Arg Tyr Ile His Leu Glu Asn Leu Leu Ala Arg Ser Tyr Phe Asp Pro Arg Glu Ala Tyr Pro Asp Gly Ser Ser Lys Glu Lys Arg Arg Ala Ala Ile Ala Gln Ala Leu Ala Gly Glu Val Ser Val Val Pro Pro Ser Arg Leu Met Ala Leu Leu Gly Gln Ala Leu Lys Trp Gln Gln His Gln Gly Leu Leu Pro Pro Gly Met Thr Ile Asp Leu Phe Arg Gly Lys Ala Ala Val Lys Asp Val Glu Glu Lys Phe Pro Thr Gln Leu Ser Arg His Ile Lys . 205 Phe Gly Gln Lys Ser His Val Glu Cys Ala Arg Phe Ser Pro Asp Gly Gln Tyr Leu Val Thr Gly Ser Val Asp Gly Phe Ile Glu Val Trp Asn Phe Thr Thr Gly Lys Ile Arg Lys Asp Leu Lys Tyr Gln Ala Gln Asp Asn Phe Met Met Asp Asp Ala Val Leu Cys Met Cys Phe Ser Arg Asp Thr Glu Met Leu Ala Thr Gly Ala Gln Asp Gly Lys Ile Lys Val Trp Lys Ile Gln Ser Gly Gln Cys Leu Arg Arg Phe Glu Arg Ala His Ser Lys Gly Val Thr Cys Leu Ser Phe Ser Lys Asp Ser Ser Gln Ile Leu Ser Ala Ser Phe Asp Gln Thr Ile Arg Ile His Gly Leu Lys Ser Gly Lys Thr Leu Lys Glu Phe Arg Gly His Ser Ser Phe Val Asn Glu Ala Thr Phe Thr Gln Asp Gly His Tyr Ile Ile Ser Ala Ser Ser Asp Gly Thr Val Lys Ile Trp Asn Met Lys Thr Thr Glu Cys Ser Asn Thr Phe Lys Ser Leu Gly Ser Thr Ala Gly Thr Asp Ile Thr Val Asn Ser Val Ile Leu Leu Pro Lys Asn Pro Glu His Phe Val Val Cys Asn Arg Ser Asn Thr Val Val Ile Met Asn Met Gln Gly Gln Ile Val Arg Ser. Phe Ser Ser Gly Lys Arg Glu Gly Gly Asp Phe Val Cys Cys Ala Leu Ser Pro Arg Gly Glu Trp Ile Tyr Cys Val Gly Glu Asp Phe Val Leu Tyr Cys Phe Ser Thr Val Thr Gly Lys Leu Glu Arg Thr Leu

```
470
                                     475
Thr Val His Glu Lys Asp Val Ile Gly Ile Ala His His Pro His
                485
                                     490
Gln Asn Leu Ile Ala Thr Tyr Ser Glu Asp Gly Leu Leu Lys Leu
                500
                                     505
Trp Lys Pro
<210> 11
<211> 186
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 722896CD1
<400> 11
Met Ile Ala Leu Phe Asn Lys Leu Leu Asp Trp Phe Lys Ala Leu
                                      10
Phe Trp Lys Glu Glu Met Glu Leu Thr Leu Val Gly Leu Gln Tyr
                 20
                                      25
Ser Gly Lys Thr Thr Phe Val Asn Val Ile Ala Ser Gly Gln Phe
                 35
                                      40
                                                          45
Asn Glu Asp Met Ile Pro Thr Val Gly Phe Asn Met Arg Lys Ile
                 50
                                      55
Thr Lys Gly Asn Val Thr Ile Lys Leu Trp Asp Ile Gly Gly Gln
                                      70
                 65
Pro Arg Phe Arg Ser Met Trp Glu Arg Tyr Cys Arg Gly Val Ser
                 80
                                      85
Ala Ile Val Tyr Met Val Asp Ala Ala Asp Gln Glu Lys Ile Glu
                 95
                                     100
Ala Ser Lys Asn Glu Leu His Asn Leu Leu Asp Lys Pro Gln Leu
                110
                                     115
Oln Gly Ile Pro Val Leu Val Leu Gly Asn Lys Arg Asp Leu Pro
                125
                                     130
Gly Ala Leu Asp Glu Lys Glu Leu Ile Glu Lys Met Asn Leu Ser
                140
                                     145
Ala Ile Gln Asp Arg Glu Ile Cys Cys Tyr Ser Ile Ser Cys Lys
                                    160
                155
Glu Lys Asp Asn Ile Asp Ile Thr Leu Gln Trp Leu Ile Gln His
                170
                                     175
Ser Lys Ser Arg Arg Ser
                185
<210> 12
<211> 204
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1571739CD1
<400> 12
Met Asn Asp Val Lys Leu Ala Val Leu Gly Gly Glu Gly Thr Gly
                                     10
Lys Ser Ala Leu Thr Val Arg Phe Leu Thr Lys Arg Phe Ile Gly
                 20
                                      25
Glu Tyr Ala Ser Asn Phe Glu Ser Ile Tyr Lys Lys His Leu Cys
                 35
                                      40
Leu Glu Arg Lys Gln Leu Asn Leu Glu Ile Tyr Asp Pro Cys Ser
                 50
                                     55
Gln Thr Gln Lys Ala Lys Phe Ser Leu Thr Ser Glu Leu His Trp
```

```
Ala Asp Gly Phe Val Ile Val Tyr Asp Ile Ser Asp Arg Ser Ser
                 80
                                      85
Phe Ala Phe Ala Lys Ala Leu Ile Tyr Arg Ile Arg Glu Pro Gln
                                     100
                 95
Thr Ser His Cys Lys Arg Ala Val Glu Ser Ala Val Phe Leu Val
                                    115
                110
                                                         120
Gly Asn Lys Arg Asp Leu Cys His Val Arg Glu Val Gly Trp Glu
                125
                                    130
Glu Gly Gln Lys Leu Ala Leu Glu Asn Arg Cys Gln Phe Cys Glu
                                    145
                                                         150
                140
Leu Ser Ala Ala Glu Gln Ser Leu Glu Val Glu Met Met Phe Ile
                                     160
                155
Arg Ile Ile Lys Asp Ile Leu Ile Asn Phe Lys Leu Lys Glu Lys
                                  175
                170
Arg Arg Pro Ser Gly Ser Lys Ser Met Ala Lys Leu Ile Asn Asn
                185
                                     190
Val Phe Gly Lys Arg Arg Lys Ser Val
                200
<210> 13
<211> 100
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1739479CD1
<400> 13
Met Trp Asp Ser Lys Lys Ile Gly Leu Arg Gln His His Cys Arg
                                     10
Lys Cys Gly Lys Ala Val Cys Gly Lys Cys Ser Ser Lys Arg Ser
                                      25
                                                          30
                 20
Ser Ile Pro Leu Met Gly Phe Glu Phe Glu Val Arg Val Cys Asp
                                      40
                                                          45
                 35
Ser Cys His Glu Ala Ile Thr Asp Glu Glu Arg Ala Pro Thr Ala
                 50
Thr Phe His Asp Ser Lys His Asn Ile Val His Val His Phe Asp
                 65
                                     70
Ala Thr Arg Gly Trp Leu Leu Thr Ser Gly Thr Asp Lys Val Ile
                 80
                                     85
Lys Leu Trp Asp Met Thr Pro Val Val Ser
                 95
<210> 14
<211> 795
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1999147CD1
<400> 14
Met Thr Ser Gly Ala Thr Arg Tyr Arg Leu Ser Cys Ser Leu Arg
                                     10
Gly His Glu Leu Asp Val Arg Gly Leu Val Cys Cys Ala Tyr Pro
                 20
                                     25
Pro Gly Ala Phe Val Ser Val Ser Arg Asp Arg Thr Thr Arg Leu
                                                          45
                 35
                                     40
Trp Ala Pro Asp Ser Pro Asn Arg Ser Phe Thr Glu Met His Cys
                 50
                                     55
                                                          60
Met Ser Gly His Ser Asn Phe Val Ser Cys Val Cys Ile Ile Pro
Ser Ser Asp Ile Tyr Pro His Gly Leu Ile Ala Thr Gly Gly Asn
```

				80					85					90
Asp	His	Asn	Ile		Ile	Phe	Ser	Leu		Ser	Pro	Met	Pro	
Tyr	Ile	Leu	Lys	Gly 110	His	Lys	Asn	Thr	Val 115	Суѕ	Ser	Leu	Ser	Ser 120
Gly	Lys	Phe	Gly	Thr 125	Leu	Leu	Ser	Gly		Trp	Asp	Thr	Thr	
Lys	Val	Trp	Leu		Asp	Lys	Cys	Met	Met 145	Thr	Leu	Gln	Gly	
Thr	Ala	Ala	Val	Trp 155	Ala	Val	Lys	Ile		Pro	Glu	Gln	Gly	
Met	Leu	Thr	Gly		Ala	Asp	Lys	Thr		Lys	Leu	Trp	Lys	
Gly	Arg	Суѕ	Glu		Thr	Phe	Ser	Gly	-:-	Glu	Asp	Cys	Val	
Gly	Leu	Ala	Ile		Ser	Glu	Thr	Glu		Leu	Ser	Cys	Ala	
Asp	Ala	Ser	Ile		Arg	Тгр	Gln	Ile		Gly	Glu	Cys	Leu	
Val	Tyr	Tyr	Gly	His 230	Thr	Asn	Tyr	Ile	Tyr 235	Ser	Ile	Ser	Val	
Pro	Asn	Cys	Arg	Asp 245	Phe	Val	Thr	Thr	Ala 250	Glu	Asp	Arg	Ser	Leu 255
Arg	Ile	Trp	Lys	His 260	Gly	Glu	Cys	Ala	Gln 265	Thr	Ile	Arg	Leu	Pro 270
Ala	Gln	Ser	Ile	Trp 275	Cys	Cys	Суѕ	Val	Leu 280	Asp	Asn	Gly	Asp	Ile 285
Val	Val	Gly	Ala	Ser 290	Asp	Gly	I·le	Ile	Arg 295	Val	Phe	Thr	Glu	Ser 300
Glu	Asp	Arg	Thr	Ala 305	Ser	Ala	Glu	Glu	Ile 310	Lys	Ala	Phe	Glu	Lys 315
Glu	Leu	Ser	His	Ala 320	Thr	Ile	Asp	Ser	Lys 325	Thr	Gly	Asp	Leu	Gly 330
Asp	Ile	Asn	Ala	Glu 335	Gln	Leu	Pro	Gly	Arg 340	Glu	His	Leu	Asn	Glu 345
Pro	Gly	Thr	Arg	Glu 350	Gly	Gln	Thr	Arg	Leu 355	Ile	Arg	Asp	Gly	Glu 360
_				365					370				Trp	375
Lys	Ile	Gly	Asp	Val 380	Val	Gly	Ser	Ser	Gly 385	Ala	Asn	Gln	Gln	Thr 390
Ser	Gly	Lys	Val	Leu 395	Tyr	Glu	Gly	Lys	Glu 400	Phe	Asp	Tyr	Val	Phe 405
Ser	Ile	Asp	Val	Asn 410	Glu	Gly	Gly	Pro	Ser 415	Tyr	Lys	Leu	Pro	Tyr 420
Asn	Thr	Ser	Asp	Asp 425	Pro	Trp	Leu	Thr	Ala 430	Tyr	Asn	Phe	Leu	Gln 435
Lys	Asn	Asp	Leu	Asn 440	Pro	Met	Phe	Leu	Asp 445	Gln	Val	Ala	Lys	Phe 450
Ile	Ile	Asp	Asn	Thr 455	Lys	Gly	Gln	Met	Leu 460	Gly	Leu	Gly	Asn	Pro 465
Ser	Phe	Ser	Asp	Pro 470	Phe	Thr	Gly	Gly	Gly 475	Arg	туг	Val	Pro	Gly 480
Ser	Ser	Gly	Ser	Ser 485	Asn	Thr	Leu	Pro	Thr 490	Ala	Asp	Pro	Phe	Thr 495
Gly	Ala	Gly	Arg	Tyr 500	Val	Pro	Gly	Ser		Ser	Met	Gly	Thr	
Met	Ala	Gly	Val		Pro	Phe	Thr	Gly		Ser	Ala	Tyr	Arg	
Ala	Ala	Ser	Lys		Met	Asn	Ile	Tyr		Pro	Lys	Lys	Glu	
Val	Thr	Phe	Asp		Ala	Asn	Pro	Thr		Ile	Leu	Gly	Lys	

Lys Glu Leu Asn Gly Thr Ala Pro Glu Glu Lys Lys Leu Thr Glu

```
560
                                     565
Asp Asp Leu Ile Leu Leu Glu Lys Ile Leu Ser Leu Ile Cys Asn
                575
                                     580
Ser Ser Ser Glu Lys Pro Thr Val Gln Gln Leu Gln Ile Leu Trp
                590
                                     595
                                                          600
Lys Ala Ile Asn Cys Pro Glu Asp Ile Val Phe Pro Ala Leu Asp
                605
                                     610
Ile Leu Arg Leu Ser Ile Lys His Pro Ser Val Asn Glu Asn Phe
                620
                                     625
Cys Asn Glu Lys Glu Gly Ala Gln Phe Ser Ser His Leu Ile Asn
                635
Leu Leu Asn Pro Lys Gly Lys Pro Ala Asn Gln Leu Leu Ala Leu
                650
                                     655
Arg Thr Phe Cys Asn Cys Phe Val Gly Gln Ala Gly Gln Lys Leu
                665
                                     670
                                                          675
Met Met Ser Gln Arg Glu Ser Leu Met Ser His Ala Ile Glu Leu
                680
                                     685
Lys Ser Gly Ser Asn Lys Asn Ile His Ile Ala Leu Ala Thr Leu
                695
                                     700
                                                         705
Ala Leu Asn Tyr Ser Val Cys Phe His Lys Asp His Asn Ile Glu
                710
                                     715
Gly Lys Ala Gln Cys Leu Ser Leu Ile Ser Thr Ile Leu Glu Val
                                                         735
                725
                                     730
Val Gln Asp Leu Glu Ala Thr Phe Arg Leu Leu Val Ala Leu Gly
                740
                                     745
                                                         750
Thr Leu Ile Ser Asp Asp Ser Asn Ala Val Gln Leu Ala Lys Ser
                755
                                    760
Leu Gly Val Asp Ser Gln Ile Lys Lys Tyr Ser Ser Val Ser Glu
                770
                                     775
                                                         780
Pro Ala Lys Val Ser Glu Cys Cys Arg Phe Ile Leu Asn Leu Leu
                785
                                     790
                                                         795
<210> 15
<211> 393
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2182085CD1
<400> 15
Met Glu Asp Phe Glu Asp Asp Pro Arg Ala Leu Gly Ala Arg Gly
                                     10
His Arg Arg Ser Val Ser Arg Gly Ser Tyr Gln Leu Gln Ala Gln
                 20
                                      25
                                                          30
Met Asn Arg Ala Val Tyr Glu Asp Arg Pro Pro Gly Ser Val Val
Pro Thr Ser Ala Ala Glu Ala Ser Arg Ala Met Ala Gly Asp Thr
                                      55
                 50
Ser Leu Ser Glu Asn Tyr Ala Phe Ala Gly Met Tyr His Val Phe
                                     70
                 65
Asp Gln His Val Asp Glu Ala Val Pro Arg Val Arg Phe Ala Asn
                 80
                                     85
Asp Asp Arg His Arg Leu Ala Cys Cys Ser Leu Asp Gly Ser Ile
                 95
                                    100
                                                         105
Ser Leu Cys Gln Leu Val Pro Ala Pro Pro Thr Val Leu Arg Val
                110
                                    115
Leu Arg Gly His Thr Arg Gly Val Ser Asp Phe Ala Trp Ser Leu
                125
                                    130
                                                         135
Ser Asn Asp Ile Leu Val Ser Thr Ser Leu Asp Ala Thr Met Arg
```

```
Ile Trp Ala Ser Glu Asp Gly Arg Cys Ile Arg Glu Ile Pro Asp
                155
                                     160
Pro Asp Ser Ala Glu Leu Leu Cys Cys Thr Phe Gln Pro Val Asn
                170
                                     175
Asn Asn Leu Thr Val Val Gly Asn Ala Lys His Asn Val His Val
                                     190
                185
                                                         195
Met Asn Ile Ser Thr Gly Lys Lys Val Lys Gly Gly Ser Ser Lys
                200
                                     205
Leu Thr Gly Arg Val Leu Ala Leu Ser Phe Asp Ala Pro Gly Arg
                215
                                     220
                                                         225
Leu Leu Trp Ala Gly Asp Asp Arg Gly Ser Val Phe Ser Phe Leu
                                     235
                230
Phe Asp Met Ala Thr Gly Lys Leu Thr Lys Ala Lys Arg Leu Val
                                     250
                245
Val His Glu Gly Ser Pro Val Thr Ser Ile Ser Ala Arg Ser Trp
                260
                                     265
                                                         270
Val Ser Arg Glu Ala Arg Asp Pro Ser Leu Leu Ile Asn Ala Cys
                275
                                     280
                                                         285
Leu Asn Lys Leu Leu Tyr Arg Val Val Asp Asn Glu Gly Thr
                                     295
                290
                                                         300
Leu Gln Leu Lys Arg Ser Phe Pro Ile Glu Gln Ser Ser His Pro
                305
                                     310
Val Arg Ser Ile Phe Cys Pro Leu Met Ser Phe Arg Gln Gly Ala
                320
                                     325
Cys Val Val Thr Gly Ser Glu Asp Met Cys Val His Phe Phe Asp
                                    340
                335
                                                         345
Val Glu Arg Ala Ala Lys Ala Ala Val Asn Lys Leu Gln Gly His
                350
                                     355
Ser Ala Pro Val Leu Asp Val Ser Phe Asn Cys Asp Glu Ser Leu
                365
                                    370
                                                         375
Leu Ala Ser Ser Asp Ala Ser Gly Met Val Ile Val Trp Arg Arg
                380
                                    385
                                                         390
Glu Gln Lys
<210> 16
<211> 485
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2216640CD1
<400> 16
Met Ala Ala Ala Val Ala Asp Glu Ala Val Ala Arg Asp Val Gln
                                     10
Arg Leu Leu Val Gln Phe Gln Asp Glu Gly Gly Gln Leu Leu Gly
Ser Pro Phe Asp Val Pro Val Asp Ile Thr Pro Asp Arg Leu Gln
                 35
Leu Val Cys Asn Ala Leu Leu Ala Gln Glu Asp Pro Leu Pro Leu
                 50
                                     55
Ala Phe Phe Val His Asp Ala Glu Ile Val Ser Ser Leu Gly Lys
                 65
                                     70
Thr Leu Glu Ser Gln Ala Val Glu Thr Glu Lys Val Leu Asp Ile
                 80
                                     85
                                                         90
Ile Tyr Gln Pro Gln Ala Ile Phe Arg Val Arg Ala Val Thr Arg
                95
                                    100
                                                        105
Cys Thr Ser Ser Leu Glu Gly His Ser Glu Ala Val Ile Ser Val
                110
                                    115
                                                        120
Ala Phe Ser Pro Thr Gly Lys Tyr Leu Ala Ser Gly Ser Gly Asp
                125
Thr Thr Val Arg Phe Trp Asp Leu Ser Thr Glu Thr Pro His Phe
```

```
140
                                     145
Thr Cys Lys Gly His Arg His Trp Val Leu Ser Ile Ser Trp Ser
                                     160
                155
Pro Asp Gly Lys Lys Leu Ala Ser Gly Cys Lys Asn Gly Gln Ile
                170
                                     175
Leu Leu Trp Asp Pro Ser Thr Gly Lys Gln Val Gly Arg Thr Leu
                185
                                     190
Ala Gly His Ser Lys Trp Ile Thr Gly Leu Ser Trp Glu Pro Leu
                200
                                     205
                                                         210
His Ala Asn Pro Glu Cys Arg Tyr Val Ala Ser Ser Ser Lys Asp
                                     220
                215
Gly Ser Val Arg Ile Trp Asp Thr Thr Ala Gly Arg Cys Glu Arg
                                                         240
                230
                                     235
Ile Leu Thr Gly His Thr Gln Ser Val Thr Cys Leu Arg Trp Gly
                                     250
                                                         255
                245
Gly Asp Gly Leu Leu Tyr Ser Ala Ser Gln Asp Arg Thr Ile Lys
                                                          270
                                     265
                260
Val Trp Arg Ala His Asp Gly Val Leu Cys Arg Thr Leu Gln Gly
                                     280
                                                         285
                275
His Gly His Trp Val Asn Thr Met Ala Leu Ser Thr Asp Tyr Ala
                                     295
                                                          300
                290
Leu Arg Thr Gly Ala Phe Glu Pro Ala Glu Ala Ser Val Asn Pro
                                                         315
                305
                                     310
Gln Asp Leu Gln Gly Ser Leu Gln Glu Leu Lys Glu Arg Ala Leu
                320
                                     325
                                                         330
Ser Arg Tyr Asn Leu Val Arg Gly Gln Gly Pro Glu Arg Leu Val
                                     340
                335
Ser Gly Ser Asp Asp Phe Thr Leu Phe Leu Trp Ser Pro Ala Glu
                                     355
                350
Asp Lys Lys Pro Leu Thr Arg Met Thr Gly His Gln Ala Leu Ile
                365
                                     370
                                                         375
Asn Gln Val Leu Phe Ser Pro Asp Ser Arg Ile Val Ala Ser Ala
                                                          390
                                     385
                380
Ser Phe Asp Lys Ser Ile Lys Leu Trp Asp Gly Arg Thr Gly Ly3
                                     400
                395
Tyr Leu Ala Ser Leu Arg Gly His Val Ala Ala Val Tyr Gln Ile
                410
                                     415
Ala Trp Ser Ala Asp Ser Arg Leu Leu Val Ser Gly Ser Ser Asp
                                     430
                                                          435
                425
Ser Thr Leu Lys Val Trp Asp Val Lys Ala Gln Lys Leu Ala Met
                                     445
                 440
Asp Leu Pro Gly His Ala Asp Glu Val Tyr Ala Val Asp Trp Ser
                                     460
                 455
                                                          465
Pro Asp Gly Gln Arg Val Ala Ser Gly Gly Lys Asp Lys Cys Leu
                                     475
                                                          480
                470
Arg Ile Trp Arg Arg
                485
<210> 17
<211> 199
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2417361CD1
<400> 17
Met Asn Pro Arg Lys Lys Val Asp Leu Lys Leu Ile Ile Val Gly
                                      10
Ala Ile Gly Val Gly Lys Thr Ser Leu Leu His Gln Tyr Val His
                                      25
                 20
Lys Thr Phe Tyr Glu Glu Tyr Gln Thr Thr Leu Gly Ala Ser Ile
```

```
Leu Ser Lys Ile Ile Ile Leu Gly Asp Thr Thr Leu Lys Leu Gln
                 50
                                     55
Ile Trp Asp Thr Gly Gly Gln Glu Arg Phe Arg Ser Met Val Ser
                 65
                                     70
Thr Phe Tyr Lys Gly Ser Asp Gly Cys Ile Leu Ala Phe Asp Val
                                     85
                 80
Thr Asp Leu Glu Ser Phe Glu Ala Leu Asp Ile Trp Arg Gly Asp
                 95
                                    100
Val Leu Ala Lys Ile Val Pro Met Glu Gln Ser Tyr Pro Met Val
                110
                                    115
Leu Leu Gly Asn Lys Ile Asp Leu Ala Asp Arg Lys Val Pro Gln
                125
                                    130
                                                         135
Glu Val Ala Gln Gly Trp Cys Arg Glu Lys Asp Ile Pro Tyr Phe
                140
                                    145
Glu Val Ser Ala Lys Asn Asp Ile Asn Val Val Gln Ala Phe Glu
                155
                                    160
Met Leu Ala Ser Arg Ala Leu Ser Arg Tyr Gln Ser Ile Leu Glu
                170
                                    175
Asn His Leu Thr Glu Ser Ile Lys Leu Ser Pro Asp Gln Ser Arg
                                    190
                185
Ser Arg Cys Cys
<210> 18
<211> 163
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2454384CD1
<400> 18
Met Glu Gly Pro Ser Leu Arg Gly Pro Ala Leu Arg Leu Ala Gly
                                     10
Leu Pro Thr Gln Gln Asp Cys Asn Ile Gln Glu Lys Ile Asp Leu
                 20
                                     25
                                                          30
Glu Ile Arg Met Arg Glu Gly Ile Trp Lys Leu Leu Ser Leu Ser
                 35
Thr Gln Lys Asp Gln Val Leu His Ala Val Lys Asn Leu Met Val
                                     55
                 50
Cys Asn Ala Arg Leu Met Ala Tyr Thr Ser Glu Leu Gln Lys Leu
                 65
                                     70
Glu Glu Gln Ile Ala Asn Gln Thr Gly Arg Cys Asp Val Lys Phe
                 80
                                     85
Glu Ser Lys Glu Arg Thr Ala Cys Lys Gly Lys Ile Ala Ile Ser
                                    100
                 95
Asp Ile Arg Ile Pro Leu Met Trp Lys Asp Ser Asp His Phe Ser
                                    115
                110
Asn Lys Glu Arg Ser Arg Arg Tyr Ala Ile Phe Cys Leu Phe Lys
                                    130
                                                         135
                125
Met Gly Ala Asn Val Phe Asp Thr Asp Val Val Asn Val Asp Lys
                                                         150
                140
                                    145
Thr Ile Thr Asp Ile Cys Phe Glu Asn Val Thr Ile Leu
<210> 19
<211> 290
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2610262CD1
```

```
<400> 19
Met Ala Ala Glu Ile Gln Pro Lys Pro Leu Thr Arg Lys Pro Ile
Leu Leu Gln Arg Met Glu Gly Ser Gln Glu Val Val Asn Met Ala
                 20
                                      25
Val Ile Val Pro Lys Glu Glu Gly Val Ile Ser Val Ser Glu Asp
                                      40
Arg Thr Val Arg Val Trp Leu Lys Arg Asp Ser Gly Gln Tyr Trp
                 50
                                      55
                                                          60
Pro Ser Val Tyr His Ala Met Pro Ser Pro Cys Ser Cys Met Ser
                                     70
Phe Asn Pro Glu Thr Arg Arg Leu Ser Ile Gly Leu Asp Asn Gly
                                      85
Thr Ile Ser Glu Phe Ile Leu Ser Glu Asp Tyr Asn Lys Met Thr
                 95
                                     100
Pro Val Lys Asn Tyr Gln Ala His Gln Ser Arg Val Thr Met Ile
                110
                                     115
Leu Phe Val Leu Glu Leu Glu Trp Val Leu Ser Thr Gly Gln Asp
                                    130
                125
Lys Gln Phe Ala Trp His Cys Ser Glu Ser Gly Gln Arg Leu Gly
                140
                                     145
Gly Tyr Arg Thr Ser Ala Val Ala Ser Gly Leu Gln Phe Asp Val
                155
                                    160
                                                         165
Glu Thr Arg His Val Phe Ile Gly Asp His Ser Gly Gln Val Thr
                170
                                    175
                                                         180
Ile Leu Lys Leu Glu Glu Glu Asn Cys Thr Leu Val Thr Thr Phe
                185
                                     190
Arg Gly His Thr Gly Gly Val Thr Ala Leu Cys Trp Asp Pro Val
                                     205
                200
Gln Arg Val Leu Phe Ser Gly Ser Ser Asp His Ser Val Ile Met
                                    220
                215
                                                         225
Trp Asp Ile Gly Gly Arg Lys Gly Thr Ala Ile Glu Leu Gln Gly
                230
                                     235
                                                         240
His Asn Asp Arg Val Gln Ala Leu Ser Tyr Ala Gln His Thr Arg
                                    250
                245
Gln Leu Ile Ser Cys Gly Gly Asp Gly Gly Ile Val Val Trp Asn
                                     265
                260
Met Asp Val Glu Arg Gln Glu Pro Leu Trp Ser Cys Phe Val Val
                275
                                    280
                                                         285
Met Ile Ser Ala Val
                290
<210> 20
<211> 705
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2700075CD1
Met Gly Thr Trp Glu His Leu Val Ser Thr Gly Phe Asn Gln Met
                                     10
Arg Glu Arg Glu Val Lys Leu Trp Asp Thr Arg Phe Phe Ser Ser
                 20
                                     25
Ala Leu Ala Ser Leu Thr Leu Asp Thr Ser Leu Gly Cys Leu Val
                 35
                                      40
Pro Leu Leu Asp Pro Asp Ser Gly Leu Leu Val Leu Ala Gly Lys
                 50
                                     55
Gly Glu Arg Gln Leu Tyr Cys Tyr Glu Val Val Pro Gln Gln Pro
                 65
                                     70
Ala Leu Ser Pro Val Thr Gln Cys Val Leu Glu Ser Val Leu Arg
```

```
Gly Ala Ala Leu Val Pro Arg Gln Ala Leu Ala Val Met Ser Cys
                                     100
                 95
Glu Val Leu Arg Val Leu Gln Leu Ser Asp Thr Ala Ile Val Pro
                110
                                     115
                                                         120
Ile Gly Tyr His Val Pro Arg Lys Ala Val Glu Phe His Glu Asp
                                     130
                125
Leu Phe Pro Asp Thr Ala Gly Cys Val Pro Ala Thr Asp Pro His
                140
                                     145
                                                         150
Ser Trp Trp Ala Gly Asp Asn Gln Gln Val Gln Lys Val Ser Leu
                                     160
                155
Asn Pro Ala Cys Arg Pro His Pro Ser Phe Thr Ser Cys Leu Val
                170
                                     175
Pro Pro Ala Glu Pro Leu Pro Asp Thr Ala Gln Pro Ala Val Met
                                     190
                185
Glu Thr Pro Val Gly Asp Ala Asp Ala Ser Glu Gly Phe Ser Ser
                                     205
                200
Pro Pro Ser Ser Leu Thr Ser Pro Ser Thr Pro Ser Ser Leu Gly
                215
                                     220
                                                         225
Pro Ser Leu Ser Ser Thr Ser Gly Ile Gly Thr Ser Pro Ser Leu
                230
                                     235
Arg Ser Leu Gln Ser Leu Leu Gly Pro Ser Ser Lys Phe Arg His
                245
                                    250
Ala Gln Gly Thr Val Leu His Arg Asp Ser His Ile Thr Asn Leu
                260
                                     265
Lys Gly Leu Asn Leu Thr Thr Pro Gly Glu Ser Asp Gly Phe Cys
                275
                                     280
Ala Asn Lys Leu Arg Val Ala Val Pro Leu Leu Ser Ser Gly Gly
                                     295
                290
Gln Val Ala Val Leu Glu Leu Arg Lys Pro Gly Arg Leu Pro Asp
                305
                                     310
Thr Ala Leu Pro Thr Leu Gln Asn Gly Ala Ala Val Thr Asp Leu
                320
                                     325
Ala Trp Asp Pro Phe Asp Pro His Arg Leu Ala Val Ala Gly Glu
                                     340
                335
Asp Ala Arg Ile Arg Leu Trp Arg Val Pro Ala Glu Gly Leu Glu
                350
                                     355
                                                         360
Glu Val Leu Thr Thr Pro Glu Thr Val Leu Thr Gly His Thr Glu
                365
Lys Ile Cys Ser Leu Arg Phe His Pro Leu Ala Ala Asn Val Leu
                                     385
                380
Ala Ser Ser Ser Tyr Asp Leu Thr Val Arg Ile Trp Asp Leu Gln
                                     400
                                                         405
                395
Ala Gly Ala Asp Arg Leu Lys Leu Gln Gly His Gln Asp Gln Ile
                                     415
                                                          420
                410
Phe Ser Leu Ala Trp Ser Pro Asp Gly Gln Gln Leu Ala Thr Val
                425
                                     430
Cys Lys Asp Gly Arg Val Arg Val Tyr Arg Pro Arg Ser Gly Pro
                440
                                     445
                                                         450
Glu Pro Leu Gln Glu Gly Pro Gly Pro Lys Gly Gly Arg Gly Ala
                                     460
                455
Arg Ile Val Trp Val Cys Asp Gly Arg Cys Leu Leu Val Ser Gly
                                     475
                470
Phe Asp Ser Gln Ser Glu Arg Gln Leu Leu Tyr Glu Ala Glu
                485
                                     490
Ala Leu Ala Gly Gly Pro Leu Ala Val Leu Gly Leu Asp Val Ala
                500
                                     505
Pro Ser Thr Leu Leu Pro Ser Tyr Asp Pro Asp Thr Gly Leu Val
                515
                                     520
                                                         525
Leu Leu Thr Gly Lys Gly Asp Thr Arg Val Phe Leu Tyr Glu Leu
                530
                                     535
Leu Pro Glu Ser Pro Phe Phe Leu Glu Cys Asn Ser Phe Thr Ser
                545
                                    550
Pro Asp Pro His Lys Gly Leu Val Leu Leu Pro Lys Thr Glu Cys
```

```
560
                                     565
Asp Val Arg Glu Val Glu Leu Met Arg Cys Leu Arg Leu Arg Gln
                575
                                     580
Ser Ser Leu Glu Pro Val Ala Phe Arg Leu Pro Arg Val Arg Lys
                                     595
                590
Glu Phe Phe Gln Asp Asp Val Phe Pro Asp Thr Ala Val Ile Trp
                                                         615
                605
                                     610
Glu Pro Val Leu Ser Ala Glu Ala Trp Leu Gln Gly Ala Asn Gly
                620
                                     625
                                                         630
Gln Pro Trp Leu Leu Ser Leu Gln Pro Pro Asp Met Ser Pro Val
                                     640
                                                         645
                635
Ser Gln Ala Pro Arg Glu Ala Pro Ala Arg Arg Ala Pro Ser Ser
                                     655
Ala Gln Tyr Leu Glu Glu Lys Ser Asp Gln Gln Lys Lys Glu Glu
                                     670
                665
Leu Leu Asn Ala Met Val Ala Lys Leu Gly Asn Arg Glu Asp Pro
                                    685
                680
Leu Pro Gln Asp Ser Phe Glu Gly Val Asp Glu Asp Glu Trp Asp
                                     700
                695
<210> 21
<211> 454
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2786701CD1
<400> 21
Met Ala Ser Ser Glu Val Ala Arg His Leu Leu Phe Gln Ser His
                                      10
Met Ala Thr Lys Thr Thr Cys Met Ser Ser Gln Gly Ser Asp Asp
                                                          30
                                     25
                 20
Glu Gln Ile Lys Arg Glu Asn Ile Arg Ser Leu Thr Met Ser Gly
                                     40
                                                          45
                 35
His Val Gly Phe Glu Ser Leu Pro Asp Gln Leu Val Asn Arg Ser
                 50
                                     55
Ile Gln Gln Gly Phe Cys Phe Asn Ile Leu Cys Val Gly Glu Thr
                 65
                                     70
Gly Ile Gly Lys Ser Thr Leu Ile Asp Thr Leu Phe Asn Thr Asn
                                     85
                 80
Phe Glu Asp Tyr Glu Ser Ser His Phe Cys Pro Asn Val Lys Leu
                                    100
                                                         105
                 95
Lys Ala Gln Thr Tyr Glu Leu Gln Glu Ser Asn Val Gln Leu Lys
                                    115
                110
                                                         120
Leu Thr Ile Val Asn Thr Val Gly Phe Gly Asp Gln Ile Asn Lys
                                                         135
                125
                                    130
Glu Glu Ser Tyr Gln Pro Ile Val Asp Tyr Ile Asp Ala Gln Phe
                140
                                    145
Glu Ala Tyr Leu Gln Glu Glu Leu Lys Ile Lys Arg Ser Leu Phe
                155
                                    160
Thr Tyr His Asp Ser Arg Ile His Val Cys Leu Tyr Phe Ile Ser
                                    175
                170
Pro Thr Gly His Ser Leu Lys Thr Leu Asp Leu Leu Thr Met Lys
                185
                                    190
Asn Leu Asp Ser Lys Val Asn Ile Ile Pro Val Ile Ala Lys Ala
                                    205
                                                         210
                200
Asp Thr Val Ser Lys Thr Glu Leu Gln Lys Phe Lys Ile Lys Leu
                215
                                    220
Met Ser Glu Leu Val Ser Asn Gly Val Gln Ile Tyr Gln Phe Pro
                230
                                    235
Thr Asp Asp Asp Thr Ile Ala Lys Val Asn Ala Ala Met Asn Gly
```

```
245
                                     250
Gln Leu Pro Phe Ala Val Val Gly Ser Met Asp Glu Val Lys Val
                260
                                     265
Gly Asn Lys Met Val Lys Ala Arg Gln Tyr Pro Trp Gly Val Val
                275
                                     280
Gln Val Glu Asn Glu Asn His Cys Asp Phe Val Lys Leu Arg Glu
                290
                                     295
Met Leu Ile Cys Thr Asn Met Glu Asp Leu Arg Glu Gln Thr His
                305
                                     310
Thr Arg His Tyr Glu Leu Tyr Arg Arg Cys Lys Leu Glu Glu Met
                320
                                     325
Gly Phe Thr Asp Val Gly Pro Glu Asn Lys Pro Val Ser Val Gln
                335
                                     340
Glu Thr Tyr Glu Ala Lys Arg His Glu Phe His Gly Glu Arg Gln
                350
                                     355
Arg Lys Glu Glu Glu Met Lys Gln Met Phe Val Gln Arg Val Lys
                                     370
                365
                                                         375
Glu Lys Glu Ala Ile Leu Lys Glu Ala Glu Arg Glu Leu Gln Ala
                380
                                     385
Lys Phe Glu His Leu Lys Arg Leu His Gln Glu Glu Arg Met Lys
                395
                                     400
                                                          405
Leu Glu Glu Lys Arg Arg Leu Leu Glu Glu Glu Ile Ile Ala Phe
                410
                                     415
                                                         420
Ser Lys Lys Lys Ala Thr Ser Glu Ile Phe His Ser Gln Ser Phe
                                     430
Leu Ala Thr Gly Ser Asn Leu Arg Lys Asp Lys Asp Arg Lys Asn
                                     445
Ser Asn Phe Leu
<210> 22
<211> 433
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3068538CD1
<400> 22
Met Ala Gly Gln Asp Pro Ala Leu Ser Thr Ser His Pro Phe Tyr
                                      10
Asp Val Ala Arg His Gly Ile Leu Gln Val Ala Gly Asp Asp Arg
                 20
                                      25
Phe Gly Arg Arg Val Val Thr Phe Ser Cys Cys Arg Met Pro Pro
                 35
                                      40
Ser His Glu Leu Asp His Gln Arg Leu Leu Glu Tyr Leu Lys Tyr
                 50
                                     55
Thr Leu Asp Gln Tyr Val Glu Asn Asp Tyr Thr Ile Val Tyr Phe
His Tyr Gly Leu Asn Ser Arg Asn Lys Pro Ser Leu Gly Trp Leu
                 80
                                     85
Gln Ser Ala Tyr Lys Glu Phe Asp Arg Lys Tyr Lys Lys Asn Leu
                 95
                                    100
Lys Ala Leu Tyr Val Val His Pro Thr Ser Phe Ile Lys Val Leu
                110
                                    115
Trp Asn Ile Leu Lys Pro Leu Ile Ser His Lys Phe Gly Lys Lys
                125
                                    130
                                                         135
Val Ile Tyr Phe Asn Tyr Leu Ser Glu Leu His Glu His Leu Lys
                140
                                    145
                                                         150
Tyr Asp Gln Leu Val Ile Pro Pro Glu Val Leu Arg Tyr Asp Glu
                155
                                    160
                                                         165
Lys Leu Gln Ser Leu His Glu Gly Arg Thr Pro Pro Pro Thr Lys
                170
```

Thr Pro Pro Pro Arg Pro Pro Leu Pro Thr Gln Gln Phe Gly Val

```
185
                                    190
Ser Leu Gln Tyr Leu Lys Asp Lys Asn Gln Gly Glu Leu Ile Pro
                200
                                    205
Pro Val Leu Arg Phe Thr Val Thr Tyr Leu Arg Glu Lys Gly Leu
                215
                                     220
Arg Thr Glu Gly Leu Phe Arg Arg Ser Ala Ser Val Gln Thr Val
                                                         240
                230
                                    235
Arg Glu Ile Gln Arg Leu Tyr Asn Gln Gly Lys Pro Val Asn Phe
                                     250
                245
Asp Asp Tyr Gly Asp Ile His Ile Pro Ala Val Ile Leu Lys Thr
                                                         270
                260
                                    265
Phe Leu Arg Glu Leu Pro Gln Pro Leu Leu Thr Phe Gln Ala Tyr
                                     280
                                                         285
                275
Glu Gln Ile Leu Gly Ile Thr Cys Val Glu Ser Ser Leu Arg Val
                                     295
                290
Thr Gly Cys Arg Gln Ile Leu Arg Ser Leu Pro Glu His Asn Tyr
                305
                                     310
                                                         315
Val Val Leu Arg Tyr Leu Met Gly Phe Leu His Ala Val Ser Arg
                320
                                     325
Glu Ser Ile Phe Asn Lys Met Asn Ser Ser Asn Leu Ala Cys Val
                335
                                    340
                                                         345
Phe Gly Leu Asn Leu Ile Trp Pro Ser Gln Gly Val Ser Ser Leu
                350
                                     355
Ser Ala Leu Val Pro Leu Asn Met Phe Thr Glu Leu Leu Ile Glu
                365
                                     370
                                                         375
Tyr Tyr Glu Lys Ile Phe Ser Thr Pro Glu Ala Pro Gly Glu His
                                     385
                380
Gly Leu Ala Pro Trp Glu Gln Gly Ser Arg Ala Ala Pro Leu Gln
                395
                                     400
                                                         405
Glu Ala Val Pro Arg Thr Gln Ala Thr Gly Leu Thr Lys Pro Thr
                                     415
                                                         420
                410
Leu Pro Pro Ser Pro Leu Met Ala Ala Arg Arg Arg Leu
                425
                                     430
<210> 23
<211> 406
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5159072CD1
<400> 23
Met Ala Asp Gly Asn Glu Asp Leu Arg Ala Asp Asp Leu Pro Gly
                                     10
Pro Ala Phe Glu Ser Tyr Glu Ser Met Glu Leu Ala Cys Pro Ala
                 20
                                      25
Glu Arg Ser Gly His Val Ala Val Ser Asp Gly Arg His Met Phe
Val Trp Gly Gly Tyr Lys Ser Asn Gln Val Arg Gly Leu Tyr Asp
                                      55
                 50
Phe Tyr Leu Pro Arg Glu Glu Leu Trp Ile Tyr Asn Met Glu Thr
                                      70
                 65
Gly Arg Trp Lys Lys Ile Asn Thr Glu Gly Asp Val Pro Pro Ser
                                      85
                 80
Met Ser Gly Ser Cys Ala Val Cys Val Asp Arg Val Leu Tyr Leu
                 95
                                     100
Phe Gly Gly His His Ser Arg Gly Asn Thr Asn Lys Phe Tyr Met
                                                         120
                110
                                     115
Leu Asp Ser Arg Ser Thr Asp Arg Val Leu Gln Trp Glu Arg Ile
                                    130
                125
Asp Cys Gln Gly Ile Pro Pro Ser Ser Lys Asp Lys Leu Gly Val
```

```
140
                                     145
Trp Val Tyr Lys Asn Lys Leu Ile Phe Phe Gly Gly Tyr Gly Tyr
                155
                                     160
                                                         165
Leu Pro Glu Asp Lys Val Leu Gly Thr Phe Glu Phe Asp Glu Thr
                170
                                     175
                                                         180
Ser Phe Trp Asn Ser Ser His Pro Arg Gly Trp Asn Asp His Val
                                     190
                185
                                                         195
His Ile Leu Asp Thr Glu Thr Phe Thr Trp Ser Gln Pro Ile Thr
                200
                                     205
Thr Gly Lys Ala Pro Ser Pro Arg Ala Ala His Ala Cys Ala Thr
                                     220
                215
Val Gly Asn Arg Gly Phe Val Phe Gly Gly Arg Tyr Arg Asp Ala
                230
                                     235
Arg Met Asn Asp Leu His Tyr Leu Asn Leu Asp Thr Trp Glu Trp
                                     250
                245
Asn Glu Leu Ile Pro Gln Gly Ile Cys Pro Val Gly Arg Ser Trp
                260
                                     265
                                                         270
His Ser Leu Thr Pro Val Ser Ser Asp His Leu Phe Leu Phe Gly
                275
                                     280
                                                         285
Gly Phe Thr Thr Asp Lys Gln Pro Leu Ser Asp Ala Trp Thr Tyr
                290
                                     295
                                                         300
Cys Ile Ser Lys Asn Glu Trp Ile Gln Phe Asn His Pro Tyr Thr
                305
                                     310
                                                         315
Glu Lys Pro Arg Leu Trp His Thr Ala Cys Ala Ser Asp Glu Gly
                320
                                     325
Glu Val Ile Val Phe Gly Gly Cys Ala Asn Asn Leu Leu Val His
                335
                                     340
                                                         345
His Arg Ala Ala His Ser Asn Glu Ile Leu Ile Phe Ser Val Gln
                350
                                     355
                                                         360
Pro Lys Ser Leu Val Arg Leu Ser Leu Glu Ala Val Ile Cys Phe
                365
                                     370
Lys Glu Met Leu Ala Asn Ser Trp Asn Cys Leu Pro Lys His Leu
                380
                                     385
Leu His Ser Val Asn Gln Arg Phe Gly Ser Asn Asn Thr Ser Gly
                395
                                     400
Ser
<210> 24
<211> 229
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5519057CD1
<400> 24
Met Ala Glu Glu Met Glu Ser Ser Leu Glu Ala Ser Phe Ser Ser
Ser Gly Ala Val Ser Gly Ala Ser Gly Phe Leu Pro Pro Ala Arg
                 20
                                     25
Ser Arg Ile Phe Lys Ile Ile Val Ile Gly Asp Ser Asn Val Gly
                 35
                                     40
                                                          45
Lys Thr Cys Leu Thr Tyr Arg Phe Cys Ala Gly Arg Phe Pro Asp
                                     55
                 50
Arg Thr Glu Ala Thr Ile Gly Val Asp Phe Arg Glu Arg Ala Val
                                     70
                 -65
Glu Ile Asp Gly Glu Arg Ile Lys Ile Gln Leu Trp Asp Thr Ala
                 80
                                     85
Gly Gln Glu Arg Phe Arg Lys Ser Met Val Gln His Tyr Tyr Arg
                 95
                                    100
Asn Val His Ala Val Val Phe Val Tyr Asp Met Thr Asn Met Ala
                110
                                    115
```

```
Ser Phe His Ser Leu Pro Ser Trp Ile Glu Glu Cys Lys Gln His
                125
                                    130
Leu Leu Ala Asn Asp Ile Pro Arg Ile Leu Val Gly Asn Lys Cys
                140
                                    145
Asp Leu Arg Ser Ala Ile Gln Val Pro Thr Asp Leu Ala Gln Lys
                155
                                    160
                                                         165
Phe Ala Asp Thr His Ser Met Pro Leu Phe Glu Thr Ser Ala Lys
                170
                                    175
                                                         180
Asn Pro Asn Asp Asn Asp His Val Glu Ala Ile Phe Met Thr Leu
                                                         195
                185
                                    190
Ala His Lys Leu Lys Cys His Lys Pro Leu Met Leu Ser Gln Pro
                                    205
Pro Asp Asn Gly Ile Ile Leu Lys Pro Glu Pro Lys Pro Ala Met
                                    220
Thr Cys Trp Cys
<210> 25
<211> 670
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 035379CD1
<400> 25
Met Ser Ser Gly Lys Ser Ala Arg Tyr Asn Arg Phe Ser Gly Gly
                                     10
Pro Ser Asn Leu Pro Thr Pro Asp Val Thr Thr Gly Thr Arg Met
                                     25
                 20
Glu Thr Thr Phe Gly Pro Ala Phe Ser Ala Val Thr Thr Ile Thr
                 35
                                     40
Lys Ala Asp Gly Thr Ser Thr Tyr Lys Gln His Cys Arg Thr Pro
                 50
                                     55
Ser Ser Ser Ser Thr Leu Ala Tyr Ser Pro Arg Asp Glu Glu Asp
                 65
Ser Met Pro Pro Ile Ser Thr Pro Arg Arg Ser Asp Ser Ala Ile
                 80
                                     85
Ser Val Arg Ser Leu His Ser Glu Ser Ser Met Ser Leu Arg Ser
                 95
                                    100
Thr Phe Ser Leu Pro Glu Glu Glu Glu Glu Pro Glu Pro Leu Val
                110
                                    115
Phe Ala Glu Gln Pro Ser Val Lys Leu Cys Cys Gln Leu Cys Cys
                                   130
                125
                                                        135
Ser Val Phe Lys Asp Pro Val Ile Thr Thr Cys Gly His Thr Phe
                140
                                    145
Cys Arg Arg Cys Ala Leu Lys Ser Glu Lys Cys Pro Val Asp Asn
                                    160
                155
Val Lys Leu Thr Val Val Val Asn Asn Ile Ala Val Ala Glu Gln
                                    175
                170
Ile Gly Glu Leu Phe Ile His Cys Arg His Gly Cys Arg Val Ala
               185
                                    190
Gly Ser Gly Lys Pro Pro Ile Phe Glu Val Asp Pro Arg Gly Cys
                200
                                    205
                                                         210
Pro Phe Thr Ile Lys Leu Ser Ala Arg Lys Asp His Glu Gly Ser
                215
                                    220
                                                         225
Cys Asp Tyr Arg Pro Val Arg Cys Pro Asn Asn Pro Ser Cys Pro
                230
                                    235
                                                        240
Pro Leu Leu Arg Met Asn Leu Glu Ala His Leu Lys Glu Cys Glu
                245
                                    250
                                                        255
His Ile Lys Cys Pro His Ser Lys Tyr Gly Cys Thr Phe Ile Gly
                                    265
Asn Gln Asp Thr Tyr Glu Thr His Leu Glu Thr Cys Arg Phe Glu
```

```
275
                                      280
 Gly Leu Lys Glu Phe Leu Gln Gln Thr Asp Asp Arg Phe His Glu
                                      295
                 290
 Met His Val Ala Leu Ala Gln Lys Asp Gln Glu Ile Ala Phe Leu
                 305
                                      310
                                                          315
 Arg Ser Met Leu Gly Lys Leu Ser Glu Lys Ile Asp Gln Leu Glu
                 320
                                      325
 Lys Ser Leu Glu Leu Lys Phe Asp Val Leu Asp Glu Asn Gln Ser
                                      340
                 335
 Lys Leu Ser Glu Asp Leu Met Glu Phe Arg Arg Asp Ala Ser Met
                 350
                                      355
 Leu Asn Asp Glu Leu Ser His Ile Asn Ala Arg Leu Asn Met Gly
                 365
                                      370
 Ile Leu Gly Ser Tyr Asp Pro Gln Gln Ile Phe Lys Cys Lys Gly
                 380
                                      385
 Thr Phe Val Gly His Gln Gly Pro Val Trp Cys Leu Cys Val Tyr
                                      400
                 395
                                                           405
 Ser Met Gly Asp Leu Leu Phe Ser Gly Ser Ser Asp Lys Thr Ile
                  410
                                      415
                                                           420
 Lys Val Trp Asp Thr Cys Thr Thr Tyr Lys Cys Gln Lys Thr Leu
                 425
                                      430
                                                           435
 Glu Gly His Asp Gly Ile Val Leu Ala Leu Cys Ile Gln Gly Cys
                                      445
                 440
                                                          450
 Lys Leu Tyr Ser Gly Ser Ala Asp Cys Thr Ile Ile Val Trp Asp
                  455
                                      460
 Ile Gln Asn Leu Gln Lys Val Asn Thr Ile Arg Ala His Asp Asn
                 470
                                      475
 Pro Val Cys Thr Leu Val Ser Ser His Asn Val Leu Phe Ser Gly
                                      490
                 485
                                                          495
 Ser Leu Lys Ala Ile Lys Val Trp Asp Ile Val Gly Thr Glu Leu
                 500
                                      505
 Lys Leu Lys Lys Glu Leu Thr Gly Leu Asn His Trp Val Arg Ala
                 515
                                      520
 Leu Vel Ala Ala Gln Ser Tyr Leu Tyr Ser Gly Ser Tyr Gln Thr
                 530
                                      535
 Ile Lys Ile Trp Asp Ile Arg Thr Leu Asp Cys Ile His Val Leu
                 545
                                      550
 Gln Thr Ser Gly Gly Ser Val Tyr Ser Ile Ala Val Thr Asn His
                                      565
                 560
 His Ile Val Cys Gly Thr Tyr Glu Asn Leu Ile His Val Trp Asp
                 575
                                      580
 Ile Glu Ser Lys Glu Gln Val Arg Thr Leu Thr Gly His Val Gly
                 590
                                      595
                                                          600
 Thr Val Tyr Ala Leu Ala Val Ile Ser Thr Pro Asp Gln Thr Lys
                 605
                                      610
 Val Phe Ser Ala Ser Tyr Asp Arg Ser Leu Arg Val Trp Ser Met
                 620
                                      625
 Asp Asn Met Ile Cys Thr Gln Thr Leu Leu Arg His Gln Ser Ser
                 635
                                      640
. Val Thr Ala Leu Ala Val Ser Arg Gly Arg Leu Phe Ser Gly Ala
                                      655
                 650
 Val Asp Ser Thr Val Lys Val Trp Thr Cys
                 665
                                      670
 <210> 26
 <211> 445
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <223> Incyte ID No: 275354CD1
```

<400> 26

```
Met Lys Val Lys Met Leu Ser Arg Asn Pro Asp Asn Tyr Val Arg
                                      10
Glu Thr Lys Leu Asp Leu Gln Arg Val Pro Arg Asn Tyr Asp Pro
                 20
Ala Leu His Pro Phe Glu Val Pro Arg Glu Tyr Val Arg Ala Leu
                 35
                                      40
Asn Ala Thr Lys Leu Glu Arg Val Phe Ala Lys Pro Phe Leu Ala
Ser Leu Asp Gly His Arg Asp Gly Val Asn Cys Leu Ala Lys His
                                     70
                 65
Pro Glu Lys Leu Ala Thr Val Leu Ser Gly Ala Cys Asp Gly Glu
Val Arg Ile Trp Asn Leu Thr Gln Arg Asn Cys Ile Arg Thr Ile
                 95
                                     100
Gln Ala His Glu Gly Phe Val Arg Gly Ile Cys Thr Arg Phe Cys
                110
                                    115
                                                         120
Gly Thr Ser Phe Phe Thr Val Gly Asp Asp Lys Thr Val Lys Gln
                125
                                    130
Trp Lys Met Asp Gly Pro Gly Tyr Gly Asp Glu Glu Glu Pro Leu
                140
                                    145
His Thr Ile Leu Gly Lys Thr Val Tyr Thr Gly Ile Asp His His
                155
                                     160
Trp Lys Glu Ala Val Phe Ala Thr Cys Gly Gln Gln Val Asp Ile
                                     175
                170
Trp Asp Glu Gln Arg Thr Asn Pro Ile Cys Ser Met Thr Trp Gly
                185
                                    190
Phe Asp Ser Ile Ser Ser Val Lys Phe Asn Pro Ile Glu Thr Phe
                200
                                    205
Leu Leu Gly Ser Cys Ala Ser Asp Arg Asn Ile Val Leu Tyr Asp
                215
                                    220
Met Arg Gln Ala Thr Pro Leu Lys Lys Val Ile Leu Asp Met Arg
                230
                                    235
                                                         240
Thr Asn Thr Ile Cys Trp Asn Pro Met Glu Ala Phe Ile Phe Thr
                245
                                    250
                                                         255
Ala Ala Asn Glu Asp Tyr Asn Leu Tyr Thr Phe Asp Met Arg Ala
                                     265
                260
Leu Asp Thr Pro Val Met Val His Met Asp His Val Ser Ala Val
                275
                                    280
Leu Asp Val Asp Tyr Ser Pro Thr Gly Lys Glu Phe Val Ser Ala
                290
                                    295
Ser Phe Asp Lys Ser Ile Arg Ile Phe Pro Val Asp Lys Ser Arg
                305
                                    310
Ser Arg Glu Val Tyr His Thr Lys Arg Met Gln His Val Ile Cys
                320
                                    325
                                                         330
Val Lys Trp Thr Ser Asp Ser Lys Tyr Ile Met Cys Gly Ser Asp
                335
                                    340
                                                         345
Glu Met Asn Ile Arg Leu Trp Lys Ala Asn Ala Ser Glu Lys Leu
                350
                                    355
Gly Val Leu Thr Ser Arg Glu Lys Ala Ala Lys Asp Tyr Asn Gln
                365
                                    370
                                                         375
Lys Leu Lys Glu Lys Phe Gln His Tyr Pro His Ile Lys Arg Ile
                380
                                    385
Ala Arg His Arg His Leu Pro Lys Ser Ile Tyr Ser Gln Ile Gln
                395
                                    400
Glu Gln Arg Ile Met Lys Glu Ala Arg Arg Arg Lys Glu Val Asn
                410
                                    415
                                                         420
Arg Ile Lys His Ser Lys Pro Gly Ser Val Pro Leu Val Ser Glu
                425
                                    430
                                                         435
Lys Lys Lys His Val Val Ala Val Val Lys
                440
                                    445
<210> 27
<211> 236
<212> PRT
```

26/115

```
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 311658CD1
<400> 27
Met Ser Asp Leu Leu Ser Pro Leu Leu Tyr Val Met Glu Asn Glu
Val Asp Ala Phe Trp Cys Phe Ala Ser Tyr Met Asp Gln Met His
                 20
Gln Asn Phe Glu Glu Gln Met Gln Gly Met Lys Thr Gln Leu Ile
Gln Leu Ser Thr Leu Leu Arg Leu Leu Asp Ser Gly Phe Cys Ser
                                     55
                 50
Tyr Leu Glu Ser Gln Asp Ser Gly Tyr Leu Tyr Phe Cys Phe Arg
                                     70
                 65
Trp Leu Leu Ile Arg Phe Lys Arg Glu Phe Ser Phe Leu Asp Ile
                 80
                                     85
Leu Arg Leu Trp Glu Val Met Trp Thr Glu Leu Pro Cys Thr Asn
                 95
                                    100
Phe His Leu Leu Cys Cys Ala Ile Leu Glu Ser Glu Lys Gln
                110
                                    115
                                                        120
Gln Ile Met Glu Lys His Tyr Gly Phe Asn Glu Ile Leu Lys His
                                    130
                125
Ile Asn Glu Leu Ser Met Lys Ile Asp Val Glu Asp Ile Leu Cys
                140
                                    145
Lys Ala Glu Ala Ile Ser Leu Gln Met Val Lys Cys Lys Glu Leu
                155
                                    160
Pro Gln Ala Val Cys Glu Ile Leu Gly Leu Gln Gly Ser Glu Val
                170
                                    175
Thr Thr Pro Asp Ser Asp Val Gly Glu Asp Glu Asn Val Val Met
                185
                                    190
                                                        195
Thr Pro Cys Pro Thr Ser Ala Phe Gln Ser Asn Ala Feu Pro Thr
                200
                                    205
                                                        210
Leu Ser Ala Ser Gly Ala Arg Asn Asp Ser Pro Thr Gln Ile Pro
                215
                                    220
Val Ser Ser Asp Val Cys Arg Leu Thr Pro Ala
                230
<210> 28
<211> 498
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1251632CD1
Met Gln Glu Ser Gly Cys Arg Leu Glu His Pro Ser Ala Thr Lys
                                     10
1
Phe Arg Asn His Val Met Glu Gly Asp Trp Asp Lys Ala Glu Asn
                20
                                     25
Asp Leu Asn Glu Leu Lys Pro Leu Val His Ser Pro His Ala Ile
                35
                                     40
Val Arg Met Lys Phe Leu Leu Gln Gln Lys Tyr Leu Glu Tyr
                50
                                     55
Leu Glu Asp Gly Lys Val Leu Glu Ala Leu Gln Val Leu Arg Cys
                65
Glu Leu Thr Pro Leu Lys Tyr Asn Thr Glu Arg Ile His Val Leu
                80
                                    85
Ser Gly Tyr Leu Met Cys Ser His Ala Glu Asp Leu Arg Ala Lys
```

```
Ala Glu Trp Glu Gly Lys Gly Thr Ala Ser Arg Ser Lys Leu Leu
                110
                                     115
Asp Lys Leu Gln Thr Tyr Leu Pro Pro Ser Val Met Leu Pro Pro
                125
                                     130
Arg Arg Leu Gln Thr Leu Leu Arg Gln Ala Val Glu Leu Gln Arg
                140
                                     145
Asp Arg Cys Leu Tyr His Asn Thr Lys Leu Asp Asn Asn Leu Asp
                155
                                     160
                                                          165
Ser Val Ser Leu Leu Ile Asp His Val Cys Ser Arg Arg Gln Phe
                170
                                     175
Pro Cys Tyr Thr Gln Gln Ile Leu Thr Glu His Cys Asn Glu Val
                185
                                     190
                                                          195
Trp Phe Cys Lys Phe Ser Asn Asp Gly Thr Lys Leu Ala Thr Gly
                200
                                     205
                                                          210
Ser Lys Asp Thr Thr Val Ile Ile Trp Gln Val Asp Pro Asp Thr
                215
                                     220
                                                          225
His Leu Leu Lys Leu Leu Lys Thr Leu Glu Gly His Ala Tyr Gly
                230
                                     235
                                                          240
Val Ser Tyr Ile Ala Trp Ser Pro Asp Asp Asn Tyr Leu Val Ala
                245
                                     250
Cys Gly Pro Asp Asp Cys Ser Glu Leu Trp Leu Trp Asn Val Gln
                                     265
                260
                                                          270
Thr Gly Glu Leu Arg Thr Lys Met Ser Gln Ser His Glu Asp Ser
                275
                                     280
                                                          285
Leu Thr Ser Val Ala Trp Asn Pro Asp Gly Lys Arg Phe Val Thr
                290
                                     295
Gly Gly Gln Arg Gly Gln Phe Tyr Gln Cys Asp Leu Asp Gly Asn
                305
                                     310
Leu Leu Asp Ser Trp Glu Gly Val Arg Val Gln Cys Leu Trp Cys
                320
                                     325
                                                          330
Leu Ser Asp Gly Lys Thr Val Leu Ala Ser Asp Thr His Gln Arg
                335
                                     340
Ile Arg Gly Tyr Asn Phe Glu Asp Leu Thr Asp Arg Asn Ile Val
                350
                                     355
                                                         360
Gln Glu Asp His Pro Ile Met Ser Phe Thr Ile Ser Lys Asn Gly
                365
                                     370
                                                          375
Arg Leu Ala Leu Leu Asn Val Ala Thr Gln Gly Val His Leu Trp
                380
                                     385
                                                          390
Asp Leu Gln Asp Arg Val Leu Val Arg Lys Tyr Gln Gly Val Thr
                395
                                     400
Gln Gly Phe Tyr Thr Ile His Ser Cys Phe Gly Gly His Asn Glu
                410
                                     415
                                                         420
Asp Phe Ile Ala Ser Gly Ser Glu Asp His Lys Val Tyr Ile Trp
                425
                                     430
                                                          435
His Lys Arg Ser Glu Leu Pro Ile Ala Glu Leu Thr Gly His Thr
                440
                                     445
                                                          450
Arg Thr Val Asn Cys Val Ser Trp Asn Pro Gln Ile Pro Ser Met
                455
                                     460
                                                         465
Met Ala Ser Ala Ser Asp Asp Gly Thr Val Arg Ile Trp Gly Pro
                470
                                     475
Ala Pro Phe Ile Asp His Gln Asn Ile Glu Glu Glu Cys Ser Ser
Met Asp Ser
<210> 29
<211> 334
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1331955CD1
```

```
<400> 29
Met Ala Thr Glu Glu Lys Lys Pro Glu Thr Glu Ala Ala Arg Ala
                  5
                                     10
Gln Pro Thr Pro Ser Ser Ser Ala Thr Gln Ser Lys Pro Thr Pro
                 20
                                      25
Val Lys Pro Asn Tyr Ala Leu Lys Phe Thr Leu Ala Gly His Thr
                 35
                                      40
Lys Ala Val Ser Ser Val Lys Phe Ser Pro Asn Gly Glu Trp Leu
                 50
Ala Ser Ser Ser Ala Asp Lys Leu Ile Lys Ile Trp Gly Ala Tyr
                 65
                                     70
Asp Gly Lys Phe Glu Lys Thr Ile Ser Gly His Lys Leu Gly Ile
Ser Asp Val Ala Trp Ser Ser Asp Ser Asn Leu Leu Val Ser Ala
                 95
                                    100
Ser Asp Asp Lys Thr Leu Lys Ile Trp Asp Val Ser Ser Gly Lys
                110
                                    115
Cys Leu Lys Thr Leu Lys Gly His Ser Asn Tyr Val Phe Cys Cys
                125
                                    130
                                                         135
Asn Phe Asn Pro Gln Ser Asn Leu Ile Val Ser Gly Ser Phe Asp
                140
                                    145
                                                         150
Glu Ser Val Arg Ile Trp Asp Val Lys Thr Gly Lys Cys Leu Lys
                155
                                    160
Thr Leu Pro Ala His Ser Asp Pro Val Ser Ala Val His Phe Asn
                                    175
                170
                                                         180
Arg Asp Gly Ser Leu Ile Val Ser Ser Ser Tyr Asp Gly Leu Cys
                185
                                     190
                                                         195
Arg Ile Trp Asp Thr Ala Ser Gly Gln Cys Leu Lys Thr Leu Ile
                200
                                    205
Asp Asp Asp Asn Pro Pro Val Ser Phe Val Lys Phe Ser Pro Asn
                215
                                    220
                                                         225
Gly Lys Tyr Ile Leu Ala Ala Thr Leu Asp Asn Thr Leu Lys Leu
                230
                                    235
                                                         240
Trp Asp Tyr Ser Lys Gly Lys Cys Leu Lys Thr Tyr Thr Gly His
                245
                                    250
Lys Asn Glu Lys Tyr Cys Ile Phe Ala Asn Phe Ser Val Thr Gly
                260
                                    265
                                                         270
Gly Lys Trp Ile Val Ser Gly Ser Glu Asp Asn Leu Val Tyr Ile
                275
                                    280
Trp Asn Leu Gln Thr Lys Glu Ile Val Gln Lys Leu Gln Gly His
                                    295
                290
Thr Asp Val Val Ile Ser Thr Ala Cys His Pro Thr Glu Asn Ile
                305
                                    310
                                                         315
Ile Ala Ser Ala Ala Leu Glu Asn Asp Lys Thr Ile Lys Leu Trp
                                    325
                320
                                                         330
Lys Ser Asp Cys
<210> 30
<211> 292
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1412614CD1
<400> 30
Met Met Ala Phe Ala Pro Pro Lys Asn Thr Asp Gly Pro Lys Met
                                     10
Gln Thr Lys Met Ser Thr Trp Thr Pro Leu Asn His Gln Leu Leu
                 20
                                     25
Asn Asp Arg Val Phe Glu Glu Arg Arg Ala Leu Leu Gly Lys Trp
```

```
Phe Asp Lys Trp Thr Asp Ser Gln Arg Arg Arg Ile Leu Thr Gly
                 50
                                     55
Leu Leu Glu Arg Cys Ser Leu Ser Gln Gln Lys Phe Cys Cys Arg
                                     70
Lys Leu Gln Glu Lys Ile Pro Ala Glu Ala Leu Asp Phe Thr Thr
                                                          90
                 80
                                     85
Lys Leu Pro Arg Val Leu Ser Leu Tyr Ile Phe Ser Phe Leu Asp
                 95
                                    100
Pro Arg Ser Leu Cys Arg Cys Ala Gln Val Cys Trp His Trp Lys
                                                         120
                110
                                    115
Asn Leu Ala Glu Leu Asp Gln Leu Trp Met Leu Lys Cys Leu Arg
                125
                                    130
Phe Asn Trp Tyr Ile Asn Phe Ser Pro Thr Pro Phe Glu Gln Gly
                140
                                    145
Ile Trp Lys Lys His Tyr Ile Gln Met Val Lys Glu Leu His Ile
                155
                                    160
Thr Lys Pro Lys Thr Pro Pro Lys Asp Gly Phe Val Ile Ala Asp
                170
                                    175
Val Gln Leu Val Thr Ser Asn Ser Pro Glu Glu Lys Gln Ser Pro
                                    190
                185
Leu Ser Ala Phe Arg Ser Ser Ser Leu Arg Lys Lys Asn Asn
                200
                                    205
Ser Gly Glu Lys Ala Leu Pro Pro Trp Arg Ser Ser Asp Lys His
                                    220
                215
Pro Thr Asp Ile Ile Arg Phe Asn Tyr Leu Asp Asn Arg Asp Pro
                230
                                    235
Met Glu Thr Val Gln Gln Gly Arg Arg Lys Arg Asn Gln Ile Thr
                245
                                    250
Pro Asp Phe Ser Arg Gln Ser His Asp Lys Lys Asn Lys Leu Gln
                260
                                    265
                                                         270
Asp Arg Thr Arg Leu Arg Lys Ala Gln Ser Met Met Ser Arg Arg
                275
                                    280
                                                         285
Asn Pro Phe Pro Leu Cys Pro
                290
<210> 31
<211> 588
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1750781CD1
<400> 31
Met Ser Ser Gly Leu Arg Ala Ala Asp Phe Pro Arg Trp Lys Arg
His Ile Ser Glu Gln Leu Arg Arg Arg Asp Arg Leu Gln Arg Gln
Ala Phe Glu Glu Ile Ile Leu Gln Tyr Asn Lys Leu Leu Glu Lys
                 35
Ser Asp Leu His Ser Val Leu Ala Gln Lys Leu Gln Ala Glu Lys
                                     55
His Asp Val Pro Asn Arg His Glu Ile Ser Pro Gly His Asp Gly
                                     70
                 65
Thr Trp Asn Asp Asn Gln Leu Gln Glu Met Ala Gln Leu Arg Ile
                 80
                                     85
Lys His Gln Glu Glu Leu Thr Glu Leu His Lys Lys Arg Gly Glu
                                    100
                 95
Leu Ala Gln Leu Val Ile Asp Leu Asn Asn Gln Met Gln Arg Lys
                110
                                    115
                                                        120
Asp Arg Glu Met Gln Met Asn Glu Ala Lys Ile Ala Glu Cys Leu
                                    130
Gln Thr Ile Ser Asp Leu Glu Thr Glu Cys Leu Asp Leu Arg Thr
```

Lvs	Leu	Cvs	Asp	140 Leu	Glu	Arg	Ala	Asn	145 Gln	Thr	Leu	Lys	Asp	150 Glu
-		-		155					160		Glu			165
_	-			170					175		Thr			180
_	-			185					190		-			195
		_		200					205		Ala			210
Lys	Asp	Ser	Arg	Arg 215	Arg	Gln	Ala	Arg	Leu 220	Gln	Lys	Glu	Leu	Ala 225
Glu	Ala	Ala	Lys	Glu 230	Pro	Leu	Pro	Val	Glu 235	Gln	Asp	Asp	Asp	Ile 240
Glu	Val	Ile	Val	Asp 245	Glu	Thr	Ser	Asp	His 250	Thr	Glu	Glu	Thr	Ser 255
Pro	Val	Arg	Ala		Ser	Arg	Ala	Ala		Arg	Arg	Ser	Val	
Ser	Phe	Pro	Val		Gln	Asp	Asn	Val		Thr	His	Pro	Gly	-
Gly	Lys	Glu	Val		Val	Pro	Ala	Thr		Leu	Cys	Val	Phe	
Ala	His	Asp	Gly		Val	Asn	Ala	Val		Phe	Ser	Pro	Gly	
Arg	Leu	Leu	Ala		Gly	Gly	Met	Asp		Arg	Val	Lys	Leu	
Glu	Val	Phe	Gly		Lys	Cys	Glu	Phe		Gly	Ser	Leu	Ser	
Ser	Asn	Ala	Gly		Thr	Ser	Ile	Glu		Asp	Ser	Ala	Gly	
Tyr	Leu	Leu	Ala		Ser	Asn	Asp	Phe		Ser	Arg	Ile	Trp	
Val	Asp	Asp	Tyr		Leu	Arg	His	Thr		Thr	Gly	His	Ser	
Lys	Val	Leu	Ser	Ala 395	Lys	Phe	Leu	Leu	Asp 400	Asn	Ala	Arg	Ile	Val 405
Ser	Gly	Ser	His	Asp 410	Arg	Thr	Leu	Lys	Leu 415	Trp	Asp	Leu	Arg	Ser 420
Lys	Val	Суѕ	Ile	Lys 425	Thr	Val	Phe	Ala	Gly 430	Ser	Ser	Суѕ	Asn	Asp 435
Ile	Val	Cys	Thr	Glu 440	Gln	Cys	Val	Met	Ser	Gly	His	Phe	Asp	Lys 450
Lys	Ile	Arg	Phe		Asp	Ile	Arg	Ser		Ser	Ile	Val	Arg	
Met	Glu	Leu	Leu		Lys	Ile	Thr	Ala		Asp	Leu	Asn	Pro	
Arg	Thr	Glu	Leu		Ser	Cys	Ser	Arg		Asp	Leu	Leu	Lys	
Ile	Asp	Leu	Arg	Thr	Asn	Ala	Ile	Lys		Thr	Phe	Ser	Ala	
Gly	Phe	Lys	Суз	500 Gly 515	Ser	Asp	Trp	Thr		Val	Val	Phe	Ser	
Asp	Gly	Ser	Tyr		Ala	Ala	Gly	Ser		Glu	Gly	Ser	Leu	
Ile	Trp	Ser	Val		Thr	Gly	Lys	Val		Lys	Val	Leu	Ser	
Gln	His	Ser	Ser		Ile	Asn	Ala	Val		Trp	Ser	Pro	Ser	
Ser	His	Val	Val		Val	Asp	Lys	Gly		Lys	Ala	Val	Leu	
Ala	Gln	Tyr		3/3					200					دەد

<210> 32 <211> 326

```
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1821658CD1
<400> 32
Met Lys Gln Asp Ala Ser Arg Asn Ala Ala Tyr Thr Val Asp Cys
Glu Asp Tyr Val His Val Val Glu Phe Asn Pro Phe Glu Asn Gly
                 20
Asp Ser Gly Asn Leu Ile Ala Tyr Gly Gly Asn Asn Tyr Val Val
                 35
Ile Gly Thr Cys Thr Phe Gln Glu Glu Glu Ala Asp Val Glu Gly
                 50
                                      55
Ile Gln Tyr Lys Thr Leu Arg Thr Phe His His Gly Val Arg Val
                                     70
                 65
Asp Gly Ile Ala Trp Ser Pro Glu Thr Arg Leu Asp Ser Leu Pro
                                     85
                 80
Pro Val Ile Lys Phe Cys Thr Ser Ala Ala Asp Met Lys Ile Arg
                 95
                                     100
Leu Phe Thr Ser Asp Leu Gln Asp Lys Asn Glu Tyr Lys Val Leu
                                                         120
                110
                                    115
Glu Gly His Thr Asp Phe Ile Asn Gly Leu Val Phe Asp Pro Lys
                                     130
                                                         135
                125
Glu Gly Gln Glu Ile Ala Ser Val Ser Asp Asp His Thr Cys Arg
                140
                                     145
Ile Trp Asn Leu Glu Gly Val Gln Thr Ala His Phe Val Leu His
                                    160
                155
                                                         165
Ser Pro Gly Met Ser Val Cys Trp His Pro Glu Glu Thr Phe Lys
                170
                                     175
                                                         180
Leu Met Val Ala Glu Lys Asn Gly Thr Ile Arg Phe Tyr Asp Leu
                                     190
                185
Leu Ala Gln Gln Ala Ile Leu Ser Leu Glu Ser Glu Gln Val Pro
                                     205
                                                         210
                200
Leu Met Ser Ala His Trp Cys Leu Lys Asn Thr Phe Lys Val Gly
                215
                                     220
                                                         225
Ala Val Ala Gly Asn Asp Trp Leu Ile Trp Asp Ile Thr Arg Ser
                230
                                     235
Ser Tyr Pro Gln Asn Lys Arg Pro Val His Met Asp Arg Ala Cys
                                     250
                245
Leu Phe Arg Trp Ser Thr Ile Ser Glu Asn Leu Phe Ala Thr Thr
                                     265
                                                         270
                260
Gly Tyr Pro Gly Lys Met Ala Ser Gln Phe Gln Ile His His Leu
                275
                                     280
Gly His Pro Gln Pro Ile Leu Met Gly Ser Val Ala Val Gly Ser
                                     295
                290
Gly Leu Ser Trp His Arg Thr Leu Pro Leu Cys Val Ile Gly Gly
                305
                                     310
                                                         315
Asp His Lys Leu Leu Phe Trp Val Thr Glu Val
                320
<210> 33
<211> 453
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1872574CD1
<400> 33
Met Ala Arg Lys Val Val Ser Arg Lys Arg Lys Ala Pro Ala Ser
```

32/115

```
Pro Gly Ala Gly Ser Asp Ala Gln Gly Pro Gln Phe Gly Trp Asp
                 20
                                      25
His Ser Leu His Lys Arg Lys Arg Leu Pro Pro Val Lys Arg Ser
Leu Val Tyr Tyr Leu Lys Asn Arg Glu Val Arg Leu Gln Asn Glu
                                      55
                 50
Thr Ser Tyr Ser Arg Val Leu His Gly Tyr Ala Ala Gln Gln Leu
Pro Ser Leu Leu Lys Glu Arg Glu Phe His Leu Gly Thr Leu Asn
                                     85
                 80
Lys Val Phe Ala Ser Gln Trp Leu Asn His Arg Gln Val Val Cys
                                     100
                                                         105
Gly Thr Lys Cys Asn Thr Leu Phe Val Val Asp Val Gln Thr Ser
                                    115
                110
Gln Ile Thr Lys Ile Pro Ile Leu Lys Asp, Arg Glu Pro Gly Gly
                125
                                     130
Val Thr Gln Gln Gly Cys Gly Ile His Ala Ile Glu Leu Asn Pro
                140
                                     145
Ser Arg Thr Leu Leu Ala Thr Gly Gly Asp Asn Pro Asn Ser Leu
                155
                                     160
Ala Ile Tyr Arg Leu Pro Thr Leu Asp Pro Val Cys Val Gly Asp
                                     175
                170
Asp Gly His Lys Asp Trp Ile Phe Ser Ile Ala Trp Ile Ser Asp
                                     190
                185
Thr Met Ala Val Ser Gly Ser Arg Asp Gly Ser Met Gly Leu Trp
                                     205
                200
Glu Val Thr Asp Asp Val Leu Thr Lys Ser Asp Ala Arg His Asn
                                     220
                215
Val Ser Arg Val Pro Val Tyr Ala His Ile Thr His Lys Ala Leu
                230
                                     235
Lys Asp Ile Pro Lys Glu Asp Thr Asn Pro Asp Asn Cys Lys Val
                                     250
                245
Arg Ala Leu Ala Phe Asn Asn Lys Asn Lys Glu Leu Gly Ala Val
                                     265
                260
Ser Leu Asp Gly Tyr Phe His Leu Trp Lys Ala Glu Asn Thr Leu
                                     280
                275
Ser Lys Leu Leu Ser Thr Lys Leu Pro Tyr Cys Arg Glu Asn Val
                                     295
                290
Cys Leu Ala Tyr Gly Ser Glu Trp Ser Val Tyr Ala Val Gly Ser
                305
                                     310
Gln Ala His Val Ser Phe Leu Asp Pro Arg Gln Pro Ser Tyr Asn
                320
                                     325
Val Lys Ser Val Cys Ser Arg Glu Arg Gly Ser Gly Ile Arg Ser
                                     340
                335
Val Ser Phe Tyr Glu His Ile Ile Thr Val Gly Thr Gly Gln Gly
                                     355
                                                         360
                350
Ser Leu Leu Phe Tyr Asp Ile Arg Ala Gln Arg Phe Leu Glu Glu
                                     370
                365
Arg Leu Ser Ala Cys Tyr Gly Ser Lys Pro Arg Leu Ala Gly Glu
                380
                                     385
Asn Leu Lys Leu Thr Thr Gly Lys Gly Trp Leu Asn His Asp Glu
                                     400
                395
Thr Trp Arg Asn Tyr Phe Ser Asp Ile Asp Phe Phe Pro Asn Ala
                410
                                     415
Val Tyr Thr His Cys Tyr Asp Ser Ser Gly Thr Lys Leu Phe Val
                425
                                     430
                                                         435
Ala Gly Gly Pro Leu Pro Ser Gly Leu His Gly Asn Tyr Ala Gly
                                     445
                                                         450
                440
Leu Trp Ser
```

<210> 34 <211> 161

```
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2590967CD1
<400> 34
Met Ala Thr Glu Gly Gly Gly Lys Glu Met Asn Glu Ile Lys Thr
Gln Phe Thr Thr Arg Glu Gly Leu Tyr Lys Leu Leu Pro His Ser
                 20
Glu Tyr Ser Arg Pro Asn Arg Val Pro Phe Asn Ser Gln Gly Ser
                                     40
Asn Pro Val Arg Val Ser Phe Val Asn Leu Asn Asp Gln Ser Gly
                 50
                                     55
Asn Gly Asp Arg Leu Cys Phe Asn Val Gly Arg Glu Leu Tyr Phe
                                     70
                 65
Tyr Ile Tyr Lys Gly Val Arg Lys Ala Ala Asp Leu Ser Lys Pro
                                     85
                 80
Ile Asp Lys Arg Ile Tyr Lys Gly Thr Gln Pro Thr Cys His Asp
                                    100
                 95
Phe Asn His Leu Thr Ala Thr Ala Glu Ser Val Ser Leu Leu Val
                110
                                    115
                                                        120
Gly Phe Ser Ala Gly Gln Val Gln Leu Ile Asp Pro Ile Lys Lys
                                    130
                                                        135
                125
Glu Thr Ser Lys Leu Phe Asn Glu Glu Gly Ser Leu Ser Ser Pro
                                   145
                140
Ser Gln Ala Ser Ser Pro Gly Gly Thr Val Val
                155
<210> 35
<211> 684
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2824491CD1
Met Ala Arg His Arg Asn Val Arg Gly Tyr Asn Tyr Asp Glu Asp
                                     10
 1
Phe Glu Asp Asp Leu Tyr Gly Gln Ser Val Glu Asp Asp Tyr
                                     25
Cys Ile Ser Pro Ser Thr Ala Ala Gln Phe Ile Tyr Ser Arg Arg
                                     40
                 35
Asp Lys Pro Ser Val Glu Pro Val Glu Glu Tyr Asp Tyr Glu Asp
                 50
                                     55
                                                         60
Leu Lys Glu Ser Ser Asn Ser Val Ser Asn His Gln Leu Ser Gly
Phe Asp Gln Ala Arg Leu Tyr Ser Cys Leu Asp His Met Arg Glu
                                     85
                 80
Val Leu Gly Asp Ala Val Pro Asp Glu Ile Leu Ile Glu Ala Val
                 95
                                    100
Leu Lys Asn Lys Phe Asp Val Gln Lys Ala Leu Ser Gly Val Leu
                110
                                    115
Glu Gln Asp Arg Val Gln Ser Leu Lys Asp Lys Asn Glu Ala Thr
                125
                                    130
                                                        135
Val Ser Thr Gly Lys Ile Ala Lys Gly Lys Pro Val Asp Ser Gln
                140
                                    145
Thr Ser Arg Ser Glu Ser Glu Ile Val Pro Lys Val Ala Lys Met
                                    160
               155
Thr Val Ser Gly Lys Lys Gln Thr Met Gly Phe Glu Val Pro Gly
```

```
170
                                    175
Val Ser Ser Glu Glu Asn Gly His Ser Phe His Thr Pro Gln Lys
                185
                                    190
Gly Pro Pro Ile Glu Asp Ala Ile Ala Ser Ser Asp Val Leu Glu
                200
                                    205
Thr Ala Ser Lys Ser Ala Asn Pro Pro His Thr Ile Gln Ala Ser
                215
                                    220
                                                         225
Glu Glu Gln Ser Ser Thr Pro Ala Pro Val Lys Lys Ser Gly Lys
                230
                                    235
                                                         240
Leu Arg Gln Gln Ile Asp Val Lys Ala Glu Leu Glu Lys Arg Gln
                                    250
                245
Gly Gly Lys Gln Leu Leu Asn Leu Val Val Ile Gly His Val Asp
                260
                                    265
Ala Gly Lys Ser Thr Leu Met Gly His Met Leu Tyr Leu Leu Gly
                                    280
                275
Asn Ile Asn Lys Arg Thr Met His Lys Tyr Glu Gln Glu Ser Lys
                                    295
                290
Lys Ala Gly Lys Ala Ser Phe Ala Tyr Ala Trp Val Leu Asp Glu
                305
                                    310
Thr Gly Glu Glu Arg Glu Arg Gly Val Thr Met Asp Val Gly Met
                320
                                    325
Thr Lys Phe Glu Thr Thr Lys Val Ile Thr Leu Met Asp Ala
                335
                                    340
Pro Gly His Lys Asp Phe Ile Pro Asn Met Ile Thr Gly Ala Ala
                350
                                    355
Gln Ala Asp Val Ala Val Leu Val Val Asp Ala Ser Arg Gly Glu
                                    370
                365
Phe Glu Ala Gly Phe Glu Thr Gly Gly Gln Thr Arg Glu His Gly
                380
                                    385
Leu Leu Val Arg Ser Leu Gly Val Thr Gln Leu Ala Val Ala Val
                395
                                    400
Asn Lys Met Asp Gln Val Asn Trp Gln Glu Arg Phe Gln Glu
                410
                                    415
                                                         420
Ile Thr Gly Lys Leu Gly His Phe Leu Lys Gln Ala Gly Phe Lys
                425
                                    430
                                                         435
Glu Ser Asp Val Gly Phe Ile Pro Thr Ser Gly Leu Ser Gly Glu
                440
                                    445
Asn Leu Ile Thr Arg Ser Gln Ser Ser Glu Leu Thr Lys Trp Tyr
                455
                                    460
Lys Gly Leu Cys Leu Leu Glu Gln Ile Asp Ser Phe Lys Pro Pro
                470
                                    475 .
Gln Arg Ser Ile Asp Lys Pro Phe Arg Leu Cys Val Ser Asp Val
                485
                                    490
                                                         495
Phe Lys Asp Gln Gly Ser Gly Phe Cys Ile Thr Gly Lys Ile Glu
                500
                                    505
Ala Gly Tyr Ile Gln Thr Gly Asp Arg Leu Leu Ala Met Pro Pro
                515
                                    520
                                                        525
Asn Glu Thr Cys Thr Val Lys Gly Ile Thr Leu His Asp Glu Pro
                530
                                    535
Val Asp Trp Ala Ala Ala Gly Asp His Val Ser Leu Thr Leu Val
                545
                                    550
Gly Met Asp Ile Ile Lys Ile Asn Val Gly Cys Ile Phe Cys Gly
                560
                                    565
                                                        570
Pro Lys Val Pro Ile Lys Ala Cys Thr Arg Phe Arg Ala Arg Ile
                575
                                    580
Leu Ile Phe Asn Ile Glu Ile Pro Ile Thr Lys Gly Phe Pro Val
                590
                                    595
                                                        600
Leu Leu His Tyr Gln Thr Val Ser Glu Pro Ala Val Ile Lys Arg
                605
                                    610
Leu Ile Ser Val Leu Asn Lys Ser Thr Gly Glu Val Thr Lys Lys
                                                        630
                620
                                    625
Lys Pro Lys Phe Leu Thr Lys Gly Gln Asn Ala Leu Val Glu Leu
                                    640
```

```
Gln Thr Gln Arg Pro Ile Ala Leu Glu Leu Tyr Lys Asp Phe Lys
                                    655
                650
Glu Leu Gly Arg Phe Met Leu Arg Tyr Gly Gly Ser Thr Ile Ala
                                    670
                665
Ala Gly Val Val Thr Glu Ile Lys Glu
                680
<210> 36
<211> 366
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2825460CD1
Met Ala Ala Ala Ala Arg Trp Asn His Val Trp Val Gly Thr
                                     10
Glu Thr Gly Ile Leu Lys Gly Val Asn Leu Gln Arg Lys Gln Ala
                                     25
Ala Asn Phe Thr Ala Gly Gly Gln Pro Arg Arg Glu Glu Ala Val
                                     40
                 35
Ser Ala Leu Cys Trp Gly Thr Gly Gly Glu Thr Gln Met Leu Val
                 50
                                     55
Gly Cys Ala Asp Arg Thr Val Lys His Phe Ser Thr Glu Asp Gly
                                     70
Ile Phe Gln Gly Gln Arg His Cys Pro Gly Gly Glu Gly Met Phe
                                     85
Arg Gly Leu Ala Gln Ala Asp Gly Thr Leu Ile Thr Cys Val Asp
                                    100
                                                         105
                 95
Ser Gly Ile Leu Arg Val Trp His Asp Lys Asp Lys Asp Thr Ser
                110
                                    115
                                                         120
Ser Asp Pro Leu Leu Glu Leu Arg Val Gly Pro Gly Val Cys Arg
                125
                                    130
Met Arg Gln Asp Pro Ala His Pro His Val Val Ala Thr Gly Gly
                                                         150
                140
                                    145
Lys Glu Asn Ala Leu Lys Ile Trp Asp Leu Gln Gly Ser Glu Glu
                155
                                    160
Pro Val Phe Arg Ala Lys Asn Val Arg Asn Asp Trp Leu Asp Leu
                170
                                    175
Arg Val Pro Ile Trp Asp Gln Asp Ile Gln Phe Leu Pro Gly Ser
                                    190
                                                         195
                185
Gln Lys Leu Val Thr Cys Thr Gly Tyr His Gln Val Arg Val Tyr
                                    205
                200
                                                         210
Asp Pro Ala Ser Pro Gln Arg Arg Pro Val Leu Glu Thr Thr Tyr
                                   · 220
                215
                                                         225
Gly Glu Tyr Pro Leu Thr Ala Met Thr Leu Thr Pro Gly Gly Asn
                                    235
                230
Ser Val Ile Val Gly Asn Thr His Gly Gln Leu Ala Glu Ile Asp
                245
                                    250
Leu Arg Gln Gly Arg Leu Leu Gly Cys Leu Lys Gly Leu Ala Gly
                260
                                    265
Ser Val Arg Gly Leu Gln Cys His Pro Ser Lys Pro Leu Leu Ala
                                    280
                275
Ser Cys Gly Leu Asp Arg Val Leu Arg Ile His Arg Ile Gln Asn
                                    295
                290
Pro Arg Gly Leu Glu His Lys Asp Glu Pro Gln Glu Pro Gln Glu
                                                        315
                305
                                    310
Pro Asn Lys Val Pro Leu Glu Asp Thr Glu Thr Asp Glu Leu Trp
                320
                                    325
Ala Ser Leu Glu Ala Ala Ala Lys Arg Lys Leu Ser Gly Leu Glu
                                    340
                335
Gln Pro Gln Gly Ala Leu Gln Thr Arg Arg Arg Lys Lys Lys Arg
```

350

```
355
                                                        360
Pro Gly Ser Thr Ser Pro
<210> 37
<211> 339
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2871116CD1
<400> 37
Met Ala Thr Glu Ile Gly Ser Pro Pro Arg Phe Phe His Met Pro
                                     10
Arg Phe Gln His Gln Ala Pro Arg Gln Leu Phe Tyr Lys Arg Pro
                 20
                                     25
Asp Phe Ala Gln Gln Gln Ala Met Gln Gln Leu Thr Phe Asp Gly
                 35
                                     40
Lys Arg Met Arg Lys Ala Val Asn Arg Lys Thr Ile Asp Tyr Asn
                 50
                                     55
Pro Ser Val Ile Lys Tyr Leu Glu Asn Arg Ile Trp Gln Arg Asp
                                     70
                65
Gln Arg Asp Met Arg Ala Ile Gln Pro Asp Ala Gly, Tyr Tyr Asn
                 80
                                     85
                                                         90
Asp Leu Val Pro Pro Ile Gly Met Leu Asn Asn Pro Met Asn Ala
                                    100
                 95
Val Thr Thr Lys Phe Val Arg Thr Ser Thr Asn Lys Val Lys Cys
                                    115
                110
                                                        120
Pro Val Phe Val Val Arg Leu Glu Glu Phe Glu Ser Leu Ser
                125
                                    130
                                                        135
Val Leu Lys Ser Trp Thr Pro Glu Gly Arg Arg Leu Val Thr Gly
                                    145
                140
Ala Ser Ser Gly Glu Phe Thr Leu Trp Asn Gly Leu Thr Phe Asn
                155
                                    160
Phe Glu Thr Ile Leu Gln Ala His Asp Ser Pro Val Arg Ala Met
                170
                                    175
Thr Trp Ser His Asn Asp Met Trp Met Leu Thr Ala Asp His Gly
                185
                                    190
Gly Tyr Val Lys Tyr Trp Gln Ser Asn Met Asn Asn Val Lys Met
                200
                                    205
                                                        210
Phe Gln Ala His Lys Glu Ala Ile Arg Glu Ala Arg Phe Ile His
                                    220
                215
                                                        225
Asn Ile Pro Phe Ser Val Val Pro Ile Val Met Val Lys Leu Phe
                230
                                    235
Ser Lys Cys Ile Leu Gly Ala Glu Met His Gly Leu Cys Gln Phe
                245
                                    250
Leu Gly Asn Phe Leu His Pro Ile Asn Thr Ile Phe Phe Val
                260
                                    265
Phe Thr His Ser Pro Phe Cys Trp His Leu Ser Glu Val Val Leu
                275
                                    280
Ser Arg Tyr Gln Pro Leu Gln Tyr Val Arg Asp Val Leu Ser Ala
                290
                                    295
Ala Phe Cys Thr Gly Phe Leu Phe Ser Phe Met Ile Asn Asn Val
                305
                                    310
Tyr Thr Leu Phe Leu Phe Ile Ile Tyr Cys Val Arg Gln Glu Tyr
               320
                                   325
                                            330
Phe Ile Pro Asn Lys Glu Phe Ser Leu
               335
<210> 38
<211> 213
<212> PRT
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<223> Incyte ID No: 2942212CD1
<400> 38
Met Glu Ala Ile Trp Leu Tyr Gln Phe Arg Leu Ile Val Ile Gly
                                     10
Asp Ser Thr Val Gly Lys Ser Cys Leu Ile Arg Arg Phe Thr Glu
Gly Arg Phe Ala Gln Val Ser Asp Pro Thr Val Gly Val Asp Phe
                                     40
Phe Ser Arg Leu Val Glu Ile Glu Pro Gly Lys Arg Ile Lys Leu
                 50
                                     55
Gln Ile Trp Asp Thr Ala Gly Gln Glu Arg Phe Arg Ser Ile Thr
                 65
                                     70
Arg Ala Tyr Tyr Arg Asn Ser Val Gly Gly Leu Leu Phe Ala
                 80
                                     85
Ile Thr Asn Arg Arg Ser Phe Gln Asn Val His Glu Trp Leu Glu
                 95
                                    100
                                                         105
Glu Thr Lys Val His Val Gln Pro Tyr Gln Ile Val Phe Val Leu
                110
                                    115
Val Gly His Lys Cys Asp Leu Asp Thr Gln Arg Gln Val Thr Arg
                125
                                    130
His Glu Ala Glu Lys Leu Ala Ala Ala Tyr Gly Met Lys Tyr Ile
                140
                                    145
Glu Thr Ser Ala Arg Asp Ala Ile Asn Val Glu Lys Ala Phe Thr
                155
                                    160
Asp Leu Thr Arg Asp Ile Tyr Glu Leu Val Lys Arg Gly Glu Ile
                170
                                    175
Thr Ile Gln Glu Gly Trp Glu Gly Val Lys Ser Gly Phe Val Pro
                185
                                    190
                                                        195
Asn Val Val His Ser Ser Glu Glu Val Val Lys Ser Glu Arg Arg
                200
                                    205
Cys Leu Cys
<210> 39
<211> 393
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3685151CD1
<400> 39
Met Glu Leu Val Ala Gly Cys Tyr Glu Gln Val Leu Phe Gly Phe
Ala Val His Pro Glu Pro Glu Ala Cys Gly Asp His Glu Gln Gln
                 20
Trp Thr Leu Val Ala Asp Phe Thr His His Ala His Thr Ala Ser
                 35
                                     40
Leu Ser Ala Val Ala Val Asn Ser Arg Phe Val Val Thr Gly Ser
                 50
                                     55
Lys Asp Glu Thr Ile His Ile Tyr Asp Met Lys Lys Ile Glu
                 65
                                     70
His Gly Ala Leu Val His His Ser Gly Thr Ile Thr Cys Leu Thr
                 80
                                     85
Phe Tyr Gly Asn Arg His Leu Ile Ser Gly Ala Glu Asp Gly Leu
                 95
                                   100
Ile Cys Ile Trp Asp Ala Lys Lys Trp Glu Ser Leu Thr Ser Ile
                110
                                                        120
                                   115
Lys Ala His Lys Gly Gln Val Thr Phe Leu Ser Ile His Pro Ser
                125
                                   130
                                                        135
```

Gly Lys Leu Ala Leu Ser Val Gly Thr Asp Lys Thr Leu Arg Thr

```
140
                                    145
Trp Asn Leu Val Glu Gly Arg Ser Ala Phe Ile Lys Asn Ile Lys
                155
                                    160
                                                         165
Gln Asn Ala His Ile Val Glu Trp Ser Pro Arg Gly Glu Gln Tyr
                                    175
                170
                                                         180
Val Val Ile Ile Gln Asn Lys Ile Asp Ile Tyr Gln Leu Asp Thr
                185
                                    190
Ala Ser Ile Ser Gly Thr Ile Thr Asn Glu Lys Arg Ile Ser Ser
                                    205
                                                         210
                200
Val Lys Phe Leu Ser Glu Ser Val Leu Ala Val Ala Gly Asp Glu
                215
Glu Val Ile Arg Phe Phe Asp Cys Asp Ser Leu Val Cys Leu Cys
                                                         240
                230
                                    235
Glu Phe Lys Ala His Glu Asn Arg Val Lys Asp Met Phe Ser Phe
                245
                                    250
                                                         255
Glu Ile Pro Glu His His Val Ile Val Ser Ala Ser Ser Asp Gly
                260
                                    265
                                                         270
Phe Ile Lys Met Trp Lys Leu Lys Gln Asp Lys Lys Val Pro Pro
                275
                                    280
                                                         285
Ser Leu Leu Cys Glu Ile Asn Thr Asn Ala Arg Leu Thr Cys Leu
                                    295
                290
Gly Val Trp Leu Asp Lys Val Ala Asp Met Lys Glu Ser Leu Pro
                                                         315
                305
                                    310
Pro Ala Ala Glu Pro Ser Pro Val Ser Lys Glu Gln Ser Lys Ile
                320
                                    325
                                                         330
Gly Lys Lys Glu Pro Gly Asp Thr Val His Lys Glu Glu Lys Arg
                335
                                    340
Ser Lys Pro Asn Thr Lys Lys Arg Gly Leu Thr Gly Asp Ser Lys
                350
                                    355
                                                         360
Lys Ala Thr Lys Glu Ser Gly Leu Ile Ser Thr Lys Lys Arg Lys
                365
                                    370
                                                         375
Met Val Glu Met Leu Glu Lys Lys Arg Lys Lys Lys Ile Lys
                                    385
                380
Thr Met Gln
<210> 40
<211> 399
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 4881515CD1
<400> 40
Met Ser Leu Gln Tyr Gly Ala Glu Glu Thr Pro Leu Ala Gly Ser
                                     10
Tyr Gly Ala Ala Asp Ser Phe Pro Lys Asp Phe Gly Tyr Gly Val
Glu Glu Glu Glu Glu Ala Ala Ala Gly Gly Gly Val Gly
                 35
                                     40
Ala Gly Ala Gly Gly Cys Gly Pro Gly Gly Ala Asp Ser Ser
                 50
                                     55
Lys Pro Arg Ile Leu Leu Met Gly Leu Arg Arg Ser Gly Lys Ser
                                     70
                 65
Ser Ile Gln Lys Val Val Phe His Lys Met Ser Pro Asn Glu Thr
                                     85
                 80
Leu Phe Leu Glu Ser Thr Asn Lys Ile Tyr Lys Asp Asp Ile Ser
                 95
                                    100
                                                        105
Asn Ser Ser Phe Val Asn Phe Gln Ile Trp Asp Phe Pro Gly Gln
                                    115
                110
Met Asp Phe Phe Asp Pro Thr Phe Asp Tyr Glu Met Ile Phe Arg
```

```
125
                                     130
Gly Thr Gly Ala Leu Ile Tyr Val Ile Asp Ala Gln Asp Asp Tyr
                140
                                     145
                                                         150
Met Glu Ala Leu Thr Arg Leu His Ile Thr Val Ser Lys Ala Tyr
                155
                                     160
                                                         165
Lys Val Asn Pro Asp Met Asn Phe Glu Val Phe Ile His Lys Val
                170
                                     175
Asp Gly Leu Ser Asp Asp His Lys Ile Glu Thr Gln Arg Asp Ile
                                     190
                                                         195
                185
His Gln Arg Ala Asn Asp Asp Leu Ala Asp Ala Gly Leu Glu Lys
                                     205
Leu His Leu Ser Phe Tyr Leu Thr Ser Ile Tyr Asp His Ser Ile
                215
                                     220
Phe Glu Ala Phe Ser Lys Val Val Gln Lys Leu Ile Pro Gln Leu
                230
                                     235
Pro Thr Leu Glu Asn Leu Leu Asn Ile Phe Ile Ser Asn Ser Gly
                                     250
                245
                                                         255
Ile Glu Lys Ala Phe Leu Phe Asp Val Val Ser Lys Ile Tyr Ile
                260
                                     265
                                                         270
Ala Thr Asp Ser Ser Pro Val Asp Met Gln Ser Tyr Glu Leu Cys
                275
                                    280
                                                         285
Cys Asp Met Ile Asp Val Val Ile Asp Val Ser Cys Ile Tyr Gly
                                     295
                                                         300
                290
Leu Lys Glu Asp Gly Ser Gly Ser Ala Tyr Asp Lys Glu Ser Met
                305
                                     310
Ala Ile Ile Lys Leu Asn Asn Thr Thr Val Leu Tyr Leu Lys Glu
                320
                                     325
Val Thr Lys Phe Leu Ala Leu Val Cys Ile Leu Arg Glu Glu Ser
                335
                                    340
Phe Glu Arg Lys Gly Leu Ile Asp Tyr Asn Phe His Cys Phe Arg
                350
                                     355
Lys Ala Ile His Glu Val Phe Glu Val Gly Val Thr Ser His Arg
                365
                                    370
Ser Cys Gly His Gln Thr Ser Ala Ser Ser Leu Lys Ala Leu Thr
                380
                                    385
His Asn Gly Thr Pro Arg Asn Ala Ile
                395
<210> 41
<211> 412
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5324681CD1
<400> 41
Met Ala Gly Ser Val Gly Leu Ala Leu Cys Gly Gln Thr Leu Val
Val Arg Gly Ser Arg Phe Leu Ala Thr Ser Ile Ala Ser Ser
Asp Asp Asp Ser Leu Phe Ile Tyr Asp Cys Ser Ala Ala Glu Lys
                 35
                                     40
Lys Ser Gln Glu Asn Lys Gly Glu Asp Ala Pro Leu Asp Gln Gly
                                     55
Ser Gly Ala Ile Leu Ala Ser Thr Phe Ser Lys Ser Gly Ser Tyr
                                     70
                 65
Phe Ala Leu Thr Asp Asp Ser Lys Arg Leu Ile Leu Phe Arg Thr
                 80
                                     85
Lys Pro Trp Gln Cys Leu Ser Val Arg Thr Val Ala Arg Arg Cys
                 95
                                    100
                                                        105
Thr Ala Leu Thr Phe Ile Ala Ser Glu Glu Lys Val Leu Val Ala
                110
                                    115
                                                         120
```

```
Asp Lys Ser Gly Asp Val Tyr Ser Phe Ser Val Leu Glu Pro His
                 125
                                     130
 Gly Cys Gly Arg Leu Glu Leu Gly His Leu Ser Met Leu Leu Asp
                 140
                                     145
 Val Ala Val Ser Pro Asp Asp Arg Phe Ile Leu Thr Ala Asp Arg
                 155
                                     160
 Asp Glu Lys Ile Arg Val Ser Trp Ala Ala Ala Pro His Ser Ile
                 170
                                     175
                                                          180
 Glu Ser Phe Cys Leu Gly His Thr Glu Phe Val Ser Arg Ile Ser
                                     190
                 185
 Val Val Pro Thr Gln Pro Gly Leu Leu Ser Ser Ser Gly Asp
                 200
                                     205
                                                          210
 Gly Thr Leu Arg Leu Trp Glu Tyr Arg Ser Gly Arg Gln Leu His
                                     220
                 215
 Cys Cys His Leu Ala Ser Leu Gln Glu Leu Val Asp Pro Gln Ala
                                     235
                 230
 Pro Gln Lys Phe Ala Ala Ser Arg Ile Ala Phe Trp Cys Gln Glu
                 245
                                     250
                                                          255
 Asn Cys Val Ala Leu Leu Cys Asp Gly Thr Pro Val Val Tyr Ile
                 260
                                     265
 Phe Gln Leu Asp Ala Arg Arg Gln Gln Leu Val Tyr Arg Gln Gln
                 275
                                     280
                                                          285
 Leu Ala Phe Gln His Gln Val Trp Asp Val Ala Phe Glu Glu Thr
                 290
                                     295
 Gln Gly Leu Trp Val Leu Gln Asp Cys Gln Glu Ala Pro Leu Val
                 305
                                     310
 Leu Tyr Arg Pro Val Gly Asp Gln Trp Gln Ser Val Pro Glu Ser
                                     325
                 320
 Thr Val Leu Lys Lys Val Ser Gly Val Leu Arg Gly Asn Trp Ala
                 335
                                     340
 Met Leu Glu Gly Ser Ala Gly Ala Asp Ala Ser Phe Ser Ser Leu
                                     355
                 350
 Tyr Lys Ala Thr Phe Asp Asn Val Thr Ser Tyr Leu Lys Lys
                                     370
                                                          375
                 365
 Glu Glu Arg Leu Gln Gln Gln Leu Glu Lys Lys Gln Arg Arg Arg
                 380
                                     385
                                                          390
 Ser Pro Pro Pro Gly Pro Asp Gly His Ala Lys Lys Met Arg Pro
                 395
                                     400
 Gly Glu Ala Thr Leu Ser Cys
                 410
 <210> 42
 <211> 163
 <212> PRT
 <213> Homo sapiens
 <220>
\ <221> misc_feature
 <223> Incyte ID No: 5387651CD1
 Met Asp Ala Leu Glu Gly Glu Ser Phe Ala Leu Ser Phe Ser Ser
                                      10
                   5
 Ala Ser Asp Ala Glu Phe Asp Ala Val Val Gly Tyr Leu Glu Asp
                  20
                                      25
 Ile Ile Met Asp Asp Glu Phe Gln Leu Leu Gln Arg Asn Phe Met
                  35
                                      40
 Asp Lys Tyr Tyr Leu Glu Phe Glu Asp Thr Glu Glu Asn Lys Leu
                  50
                                      55
                                                          60
 Ile Tyr Thr Pro Ile Phe Asn Glu Tyr Ile Ser Leu Val Glu Lys
                  65
                                      70
 Tyr Ile Glu Glu Gln Leu Leu Gln Arg Ile Pro Glu Phe Asn Met
                  80
                                      85
 Ala Ala Phe Thr Thr Leu Gln His His Lys Asp Glu Val Ala
```

```
95
                                     100
Gly Asp Ile Ph Asp Met Leu Leu Thr Phe Thr Asp Phe Leu Ala
                                     115
                110
Phe Lys Glu Met Phe Leu Asp Tyr Arg Ala Glu Lys Glu Gly Arg
                125
                                     130
                                                          135
Gly Leu Asp Leu Ser Ser Gly Leu Val Val Thr Ser Leu Cys Lys
                140
                                     145
                                                         150
Ser Ser Ser Leu Pro Ala Ser Gln Asn Asn Leu Arg His
                155
                                     160
<210> 43
<211> 514
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5595679CD1
<400> 43
Met Gln Glu Ser Gly Cys Arg Leu Glu His Pro Ser Ala Thr Lys
                                      10
Phe Arg Asn His Val Met Glu Gly Asp Trp Asp Lys Ala Glu Asn
                 20
                                      25
Asp Leu Asn Glu Leu Lys Pro Leu Val His Ser Pro His. Ala Ile
Val Val Arg Gly Ala Leu Glu Ile Ser Gln Thr Leu Leu Gly Ile
                 50
                                      55
Ile Val Arg Met Lys Phe Leu Leu Gln Gln Lys Tyr Leu Glu
                 65
                                      70
Tyr Leu Glu Asp Gly Lys Val Leu Glu Ala Leu Gln Val Leu Arg
                 80
                                      85
Cys Glu Leu Thr Pro Leu Lys Tyr Asn Thr Glu Arg Ile His Val
                 95
                                     100
Leu Ser Gly Tyr Leu Met Cys Ser His Ala Glu Asp Leu Arg Ala
                110
                                     115
                                                         120
Lys Ala Glu Trp Glu Gly Lys Gly Thr Ala Ser Arg Ser Lys Leu
                125
                                     130
Leu Asp Lys Leu Gln Thr Tyr Leu Pro Pro Ser Val Met Leu Pro
                140
                                     145
Pro Arg Arg Leu Gln Thr Leu Leu Arg Gln Ala Val Glu Leu Gln
                155
                                     160
Arg Asp Arg Cys Leu Tyr His Asn Thr Lys Leu Asp Asn Asn Leu
                170
                                     175
Asp Ser Val Ser Leu Leu Ile Asp His Val Cys Ser Arg Arg Gln
                185
                                     190
Phe Pro Cys Tyr Thr Gln Gln Ile Leu Thr Glu His Cys Asn Glu
                200
                                    205
                                                         210
Val Trp Phe Cys Lys Phe Ser Asn Asp Gly Thr Lys Leu Ala Thr
                215
                                     220
Gly Ser Lys Asp Thr Thr Val Ile Ile Trp Gln Val Asp Pro Asp
                230
                                     235
                                                         240
Thr His Leu Leu Lys Leu Leu Lys Thr Leu Glu Gly His Ala Tyr
                                    250
                245
                                                         255
Gly Val Ser Tyr Ile Ala Trp Ser Pro Asp Asp Asn Tyr Leu Val
                260
                                    265
Ala Cys Gly Pro Asp Asp Cys Ser Glu Leu Trp Leu Trp Asn Val
                275
                                    280
                                                         285
Gln Thr Gly Glu Leu Arg Thr Lys Met Ser Gln Ser His Glu Asp
                290
                                    295
Ser Leu Thr Ser Val Ala Trp Asn Pro Asp Gly Lys Arg Phe Val
                305
                                    310
                                                         315
Thr Gly Gly Gln Arg Gly Gln Phe Tyr Gln Cys Asp Leu Asp Gly
                320
                                    325
                                                         330
```

```
Asn Leu Leu Asp Ser Trp Glu Gly Val Arg Val Gln Cys Leu Trp
                335
                                    340
Cys Leu Ser Asp Gly Lys Thr Val Leu Ala Ser Asp Thr His Gln
                350
                                    355
Arg Ile Arg Gly Tyr Asn Phe Glu Asp Leu Thr Asp Arg Asn Ile
                365
                                    370
Val Gln Glu Asp His Pro Ile Met Ser Phe Thr Ile Ser Lys Asn
                380
                                    385
Gly Arg Leu Ala Leu Leu Asn Val Ala Thr Gln Gly Val His Leu
                395
                                    400
Trp Asp Leu Gln Asp Arg Val Leu Val Arg Lys Tyr Gln Gly Val
                410
                                    415
Thr Gln Gly Phe Tyr Thr Ile His Ser Cys Phe Gly Gly His Asn
                425
                                    430
Glu Asp Phe Ile Ala Ser Gly Ser Glu Asp His Lys Val Tyr Ile
                440
                                    445
                                                         450
Trp His Lys Arg Ser Glu Leu Pro Ile Ala Glu Leu Thr Gly His
                455
                                    460
Thr Arg Thr Val Asn Cys Val Ser Trp Asn Pro Gln Ile Pro Ser
                470
                                    475
                                                         480
Met Met Ala Ser Ala Ser Asp Asp Gly Thr Val Arg Ile Trp Gly
                485
                                    490
                                                         495
Pro Ala Pro Phe Ile Asp His Gln Asn Ile Glu Glu Glu Cys Ser
                500
Ser Met Asp Ser
<210> 44
<211> 67
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5782457CD1
Met Glu Glu Trp Asp Val Pro Gln Met Lys Lys Glu Val Glu Ser
                                     10
1
Leu Lys Tyr Gln Leu Ala Phe Gln Arg Glu Met Ala Ser Lys Thr
                 20
                                     25
Ile Pro Glu Leu Leu Lys Trp Ile Glu Asp Gly Ile Pro Lys Asp
                 35
                                     40
Pro Phe Leu Asn Pro Asp Leu Met Lys Asn Asn Pro Trp Val Glu
                 50
Lys Gly Lys Cys Thr Ile Leu
                 65
<210> 45
<211> 315
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 760677CD1
<400> 45
Met Ala Phe Pro Glu Pro Lys Pro Arg Pro Pro Glu Leu Pro Gln
Lys Arg Leu Lys Thr Leu Asp Cys Gly Gln Gly Ala Val Arg Ala
                 20
                                     25
                                                         30
Val Arg Phe Asn Val Asp Gly Asn Tyr Cys Leu Thr Cys Gly Ser
Asp Lys Thr Leu Lys Leu Trp Asn Pro Leu Arg Gly Thr Leu Leu
```

Arg Thr Tyr Ser Gly His Gly Tyr Glu Val Leu Asp Ala Ala Gly

50

```
70
                 65
Ser Phe Asp Asn Ser Ser Leu Cys Ser Gly Gly Asp Lys Ala
                 80
                                      85
Val Val Leu Trp Asn Val Ala Ser Gly Gln Val Val Arg Lys Phe
                 95
                                    100
Arg Gly His Ala Gly Lys Val Asn Thr Val Gln Phe Ser Glu Glu
                                    115
                                                         120
                110
Ala Thr Val Ile Leu Ser Gly Ser Ile Asp Ser Ser Ile Arg Cys
                125
                                     130
Trp Asp Cys Arg Ser Arg Arg Pro Glu Pro Val Gln Thr Leu Asp
                140
                                    145
Glu Ala Arg Asp Gly Val Ser Ser Val Lys Val Ser Asp His Glu
                155
                                    160
Ile Leu Ala Gly Ser Val Asp Gly Arg Val Arg Arg Tyr Asp Leu
                170
                                    175
                                                         180
Arg Met Gly Gln Leu Phe Ser Asp Tyr Val Gly Ser Pro Ile Thr
                185
                                    190
Cys Thr Cys Phe Ser Arg Asp Gly Gln Cys Thr Leu Val Ser Ser
                200
                                     205
Leu Asp Ser Thr Leu Arg Leu Leu Asp Lys Asp Thr Gly Glu Leu
                                    220
                                                         225
                215
Leu Gly Glu Tyr Lys Gly His Lys Asn Gln Glu Tyr Lys Leu Asp
                230
                                     235
Cys Cys Leu Ser Glu Arg Asp Thr His Val Val Ser Cys Ser Glu
                                     250
                245
Asp Gly Lys Val Phe Phe Trp Asp Leu Val Glu Gly Ala Leu Ala
                                    265
                260
                                                         270
Leu Ala Leu Pro Val Gly Ser Gly Val Val Gln Ser Leu Asp Tyr
                275
                                    280
                                                         285
His Pro Thr Glu Pro Cys Leu Leu Thr Ala Met Gly Gly Ser Val
                                    295
                290
Gln Cys Trp Arg Glu Glu Ala Tyr Glu Ala Glu Asp Gly Ala Gly
                                    310
<210> 46
<211> 504
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1348567CD1
<400> 46
Met Ser Leu Ile Cys Ser Ile Ser Asn Glu Val Pro Glu His Pro
Cys Val Ser Pro Val Ser Asn His Val Tyr Glu Arg Arg Leu Ile
                                     25
Glu Lys Tyr Ile Ala Glu Asn Gly Thr Asp Pro Ile Asn Asn Gln
                 35
                                     40
Pro Leu Ser Glu Glu Gln Leu Ile Asp Ile Lys Val Ala His Pro
                                     55
                 50
Ile Arg Pro Lys Pro Pro Ser Ala Thr Ser Ile Pro Ala Ile Leu
                 65
                                     70
Lys Ala Leu Gln Asp Glu Trp Asp Ala Val Met Pro His Ser Phe
                 80
                                     85
Thr Leu Arg Gln Gln Leu Gln Thr Thr Arg Gln Glu Leu Ser His
                95
                                    100
                                                        105
Ala Leu Tyr Gln His Asp Ala Ala Cys Arg Val Ile Ala Arg Leu
                110
                                    115
Thr Lys Glu Val Thr Ala Ala Arg Glu Ala Leu Ala Thr Leu Lys
```

```
125
                                     130
Pro Gln Ala Gly Leu Ile Val Pro Gln Ala Val Pro Ser Ser Gln
                 140
                                     145
Pro Ser Val Val Gly Ala Gly Glu Pro Met Asp Leu Gly Glu Leu
                 155
                                     160
Val Gly Met Thr Pro Glu Ile Ile Gln Lys Leu Gln Asp Lys Ala
                170
                                     175
Thr Val Leu Thr Thr Glu Arg Lys Lys Arg Gly Lys Thr Val Pro
                 185
                                     190
Glu Glu Leu Val Lys Pro Glu Glu Leu Ser Lys Tyr Arg Gln Val
                 200
                                     205
Ala Ser His Val Gly Leu His Ser Ala Ser Ile Pro Gly Ile Leu
                215
                                     220
Ala Leu Asp Leu Cys Pro Ser Asp Thr Asn Lys Ile Leu Thr Gly
                230
                                     235
Gly Ala Asp Lys Asn Val Val Val Phe Asp Lys Ser Ser Glu Gln
                245
                                     250
Ile Leu Ala Thr Leu Lys Gly His Thr Lys Lys Val Thr Ser Val
                260
                                     265
                                                          270
Val Phe His Pro Ser Gln Asp Leu Val Phe Ser Ala Ser Pro Asp
                275
                                     280
                                                         285
Ala Thr Ile Arg Ile Trp Ser Val Pro Asn Ala Ser Cys Val Gln
                 290
                                     295
Val Val Arg Ala His Glu Ser Ala Val Thr Gly Leu Ser Leu His
                305
                                     310
Ala Thr Gly Asp Tyr Leu Leu Ser Ser Ser Asp Asp Gln Tyr Trp
                                     325
                320
Ala Phe Ser Asp Ile Gln Thr Gly Arg Val Leu Thr Lys Val Thr
                335
                                     340
Asp Glu Thr Ser Gly Cys Ser Leu Thr Cys Ala Gln Phe His Pro
                350
                                     355
Asp Gly Leu Ile Phe Gly Thr Gly Thr Met Asp Ser Gln Ile Lys
                365
                                     370
                                                         375
Ile Trp Asp Leu Lys Glu Arg Thr Asn Val Ala Asn Phe Pro Gly
                                     385
                380
                                                         390
His Ser Gly Pro Ile Thr Ser Ile Ala Phe Ser Glu Asn Gly Tyr
                395
                                     400
Tyr Leu Ala Thr Ala Ala Asp Asp Ser Ser Val Lys Leu Trp Asp
                410
                                     415
Leu Arg Lys Leu Lys Asn Phe Lys Thr Leu Gln Leu Asp Asn Asn
                425
                                     430
Phe Glu Val Lys Ser Leu Ile Phe Asp Gln Ser Gly Thr Tyr Leu
                440
                                     445
                                                         450
Ala Leu Gly Gly Thr Asp Val Gln Ile Tyr Ile Cys Lys Gln Trp
                455
                                     460
                                                         465
Thr Glu Ile Leu His Phe Thr Glu His Ser Gly Leu Thr Thr Gly
                470
                                     475
Val Ala Phe Gly His His Ala Lys Phe Ile Ala Ser Thr Gly Met
                485
Asp Arg Ser Leu Lys Phe Tyr Ser Leu
                500
<210> 47
<211> 522
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1751354CD1
<400> 47
Met Ala Phe Leu Asp Asn Pro Thr Ile Ile Leu Ala His Ile Arg
```

Gln Ser His Val Thr Ser Asp Asp Thr Gly Met Cys Glu Met Val Leu Ile Asp His Asp Val Asp Leu Glu Lys Ile His Pro Pro Ser Met Pro Gly Asp Ser Gly Ser Glu Ile Gln Gly Ser Asn Gly Glu Thr Gln Gly Tyr Val Tyr Ala Gln Ser Val Asp Ile Thr Ser Ser Trp Asp Phe Gly Ile Arg Arg Ser Asn Thr Ala Gln Arg Leu Glu Arg Leu Arg Lys Glu Arg Gln Asn Gln Ile Lys Cys Lys Asn Ile Gln Trp Lys Glu Arg Asn Ser Lys Gln Ser Ala Gln Glu Leu Lys Ser Leu Phe Glu Lys Lys Ser Leu Lys Glu Lys Pro Pro Ile Ser Gly Lys Gln Ser Ile Leu Ser Val Arg Leu Glu Gln Cys Pro Leu Gln Leu Asn Asn Pro Phe Asn Glu Tyr Ser Lys Phe Asp Gly Lys Gly His Val Gly Thr Thr Ala Thr Lys Lys Ile Asp Val Tyr Leu Pro Leu His Ser Ser Gln Asp Arg Leu Leu Pro Met Thr Val Val Thr Met Ala Ser Ala Arg Val Gln Asp Leu Ile Gly Leu Ile Cys Trp Gln Tyr Thr Ser Glu Gly Arg Glu Pro Lys Leu Asn Asp Asn Val Ser Ala Tyr Cys Leu His Ile Ala Glu Asp Asp Gly Glu Val Asp Thr Asp Phe Pro Pro Leu Asp Ser Asn Glu Pro Ile His Lys Phe Gly Phe Ser Thr Leu Ala Leu Val Glu Lys Tyr Ser Ser Pro Gly Leu Thr Ser Lys Glu Ser Leu Phe Val Arg Ile Asn Ala Ala His Gly Phe Ser Leu Ile Gln Val Asp Asn Thr Lys Val Thr Met Lys Glu Ile Leu Leu Lys Ala Val Lys Arg Arg Lys Gly Ser Gln Lys Val Ser Gly Pro Gln Tyr Arg Leu Glu Lys Gln Ser Glu Pro Asn Val Ala Val Asp Leu Asp Ser Thr Leu Glu Ser Gln Ser Ala Trp Glu Phe Cys Leu Val Arg Glu Asn Ser Ser Arg Ala Asp Gly Val Phe Glu Glu Asp Ser Gln Ile Asp Ile Ala Thr Val Gln Asp Met Leu Ser Ser His His Tyr Lys Ser Phe Lys Val Ser Met Ile His Arg Leu Arg Phe Thr Thr Asp Val Gln Leu Gly Ile Ser Gly Asp Lys Val Glu Ile Asp Pro Val Thr Asn Gln Lys Ala Ser Thr Lys Phe Trp Ile Lys Gln Lys Pro Ile Ser Ile Asp Ser Asp Leu Leu Cys Ala Cys Asp Leu Ala Glu Glu Lys Ser Pro Ser His Ala Ile Phe Lys Leu Thr Tyr Leu Ser Asn His Asp Tyr Lys His Leu Tyr Phe Glu Ser Asp Ala Ala Thr Val Asn Glu Ile Val Leu Lys Val Asn Tyr Ile Leu Glu Ser Arg Ala Ser Thr Ala Arg Ala

```
485
                                    490
Asp Tyr Phe Ala Gln Lys Gln Arg Lys Leu Asn Arg Arg Thr Ser
                500
                                    505
Phe Ser Phe Gln Lys Glu Lys Lys Ser Gly Gln Gln
<210> 48
<211> 316
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1976780CD1
<400> 48
Met Ala Ser Lys Asp Lys Ser Ser Lys Lys Asn Val Phe Glu Leu
                                     10
Lys Thr Arg Gln Gly Thr Glu Leu Leu Ile Gln Ser Asp Asn Asp
                 20
                                     25
Thr Val Ile Asn Asp Trp Phe Lys Val Leu Ser Ser Thr Ile Asn
                 35
                                      40
Asn Gln Ala Val Glu Thr Asp Glu Gly Ile Glu Glu Glu Ile Pro
                                     55
                                                          60
                 50
Asp Ser Pro Gly Ile Glu Lys His Asp Lys Glu Lys Glu Gln Lys
                 65
Asp Pro Lys Lys Leu Arg Ser Phe Lys Val Ser Ser Ile Asp Ser
                 80
                                     85
Ser Glu Gln Lys Lys Thr Lys Lys Asn Leu Lys Lys Phe Leu Thr
                                    100
                 95
Arg Arg Pro Thr Leu Gln Ala Val Arg Glu Lys Gly Tyr Ile Lys
                110
                                    115
                                                         120
Asp Gln Val Phe Gly Ser Asn Leu Ala Asn Leu Cys Gln Arg Glu
                                                         135
                125
                                    130
Asn Gly Thr Val Pro Lys Phe Val Lys Leu Cys Ile Glu His Val
                                    145
                140
Glu Glu His Gly Leu Asp Ile Asp Gly Ile Tyr Arg Val Ser Gly
                                    160
                155
Asn Leu Ala Val Ile Gln Lys Leu Arg Phe Ala Val Asn His Asp
                                    175
                170
Glu Lys Leu Asp Leu Asn Asp Ser Lys Trp Glu Asp Ile His Val
                185
                                    190
Ile Thr Gly Ala Leu Lys Met Phe Phe Arg Glu Leu Pro Glu Pro
                200
                                    205
Leu Phe Thr Phe Asn His Phe Asn Asp Phe Val Asn Ala Ile Lys
                                                         225
                                    220
                215
Gln Glu Pro Arg Gln Arg Val Ala Ala Val Lys Asp Leu Ile Arg
                230
                                    235
                                                         240
Gln Leu Pro Lys Pro Asn Gln Asp Thr Met Gln Ile Leu Phe Arg
                                    250
                                                         255
                245
His Leu Arg Arg Val Ile Glu Asn Gly Glu Lys Asn Arg Met Thr
                260
                                    265
Tyr Gln Ser Ile Ala Ile Val Phe Gly Pro Thr Leu Leu Lys Pro
                                    280
                275
Glu Lys Glu Thr Gly Asn Ile Ala Val His Thr Val Tyr Gln Asn
                290
                                    295
                                                         300
Gln Ile Val Glu Leu Ile Leu Leu Glu Leu Ser Ser Ile Phe Gly
                305
                                    310
                                                         315
Arg
<210> 49
<211> 387
<212> PRT
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<223> Incyte ID No: 2048234CD1
<400> 49
Met Val His Cys Ser Cys Val Leu Phe Arg Lys Tyr Gly Asn Phe
                                     10
Ile Asp Lys Leu Arg Leu Phe Thr Arg Gly Gly Ser Gly Gly Met
Gly Tyr Pro Arg Leu Gly Gly Glu Gly Gly Lys Gly Gly Asp Val
                                     40
                 35
Trp Val Val Ala Gln Asn Arg Met Thr Leu Lys Gln Leu Lys Asp
                                                          60
Arg Tyr Pro Arg Lys Arg Phe Val Ala Gly Val Gly Ala Asn Ser
                                     70
                 65
Lys Ile Ser Ala Leu Lys Gly Ser Lys Gly Lys Asp Trp Glu Ile
                 80
                                     85
Pro Val Pro Val Gly Ile Ser Val Thr Asp Glu Asn Gly Lys Ile
                                    100
                 95
Ile Gly Glu Leu Ser Lys Glu Asn Asp Arg Ile Leu Val Ala Gln
                110
                                    115
Gly Gly Leu Gly Gly Lys Leu Leu Thr Asn Phe Leu Pro Leu Lys
                                    130
                                                         135
                125
Gly Gln Lys Arg Ile Ile His Leu Asp Leu Lys Leu Ile Ala Asp
                                    145
                140
Val Gly Leu Val Gly Phe Pro Asn Ala Gly Lys Ser Ser Leu Leu
                                    .160
                155
Ser Cys Val Ser His Ala Lys Pro Ala Ile Ala Asp Tyr Ala Phe
                170
                                    175
Thr Thr Leu Lys Leu Lys Leu Gly Lys Ile Met Tyr Ser Asp Phe
                185
                                    190
Lys Gln Ile Ser Val Ala Asp Leu Pro Gly Leu Ile Glu Gly Ala
                                    205
                200
His Met Asn Lys Gly Met Gly His Lys Phe Leu Lys His Ile Glu
                215
                                    220
Arg Thr Arg Gln Leu Leu Phe Val Val Asp Ile Ser Gly Phe Gln
                                    235
                230
Leu Ser Ser His Thr Gln Tyr Arg Thr Ala Phe Glu Thr Ile Ile
                                    250
                245
Leu Leu Thr Lys Glu Leu Glu Leu Tyr Lys Glu Glu Leu Gln Thr
                                                         270
                260
                                    265
Lys Pro Ala Leu Leu Ala Val Asn Lys Met Asp Leu Pro Asp Ala
                                    280
                                                         285
                275
Gln Asp Lys Phe His Glu Leu Met Ser Gln Leu Gln Asn Pro Lys
                                    295
                290
Asp Phe Leu His Leu Phe Glu Lys Asn Met Ile Pro Glu Arg Thr
                305
                                    310
                                                         315
Val Glu Phe Gln His Ile Ile Pro Ile Ser Ala Val Thr Gly Glu
                                    325
                320
Gly Ile Glu Glu Leu Lys Asn Cys Ile Arg Lys Ser Leu Asp Glu
                                    340
                335
Gln Ala Asn Gln Glu Asn Asp Ala Leu His Lys Lys Gln Leu Leu
                350
                                    355
Asn Leu Trp Ile Ser Asp Thr Met Ser Ser Thr Glu Pro Pro Ser
                365
                                    370
Lys His Ala Val Thr Thr Ser Lys Met Asp Ile Ile
                380
                                    385
<210> 50
<211> 334
<212> PRT
<213> Homo sapiens
```

<220>

<221> misc_feature <223> Incyte ID No: 2111754CD1 <400> 50 Met Pro Ser Gly Pro Arg Ala Ala Leu Arg Trp Ala Ser Pro Ser 10 Gln Leu Val Ser Tyr His Val Leu Arg Asn Gly Ile Tyr Ala Cys 20 25 Tyr Pro His Ser Leu Arg Pro Arg Thr Pro Leu Leu Cys Ala Ser 45 35 40 Arg Asn Ile Lys Pro Arg Arg Ser Glu Leu Leu Gly Cys Pro Val 55 50 Gly Cys Arg Gly Ser Leu Ser Glu Gln Arg Ile Cys Leu Leu Gly 70 Cys Leu Val Arg Ala Ser Glu Lys Gly Val Ser Cys Cys Gln Leu 80 85 Ser Val Gly Glu Leu Val His Val Ser Pro Leu Arg Ile Pro Thr 100 95 Met Gly Asn Ala Ser Phe Gly Ser Lys Glu Gln Lys Leu Leu Lys 115 110 120 Arg Leu Arg Leu Leu Pro Ala Leu Leu Ile Leu Arg Ala Phe Lys 130 135 125 Pro His Arg Lys Ile Arg Asp Tyr Arg Val Val Val Gly Thr 140 145 150 Ala Gly Val Gly Lys Ser Thr Leu Leu His Lys Trp Ala Ser Gly 155 160 Asn Phe Arg His Glu Tyr Leu Pro Thr Ile Glu Asn Thr Tyr Cys 175 170 Gln Leu Leu Gly Cys Ser His Gly Val Leu Ser Leu His Ile Thr 185 190 195 Asp Ser Lys Ser Gly Asp Gly Asn Arg Ala Leu Gln Arg His Val 205 210 200 Ile Ala Arg Gly His Ala Phe Val Leu Val Tyr Ser Val Thr Lys 220 225 215 Lys Glu Thr Leu Glu Glu Leu Lys Ala Phe Tyr Glu Leu Ile Cys 230 235 240 Lys Ile Lys Gly Asn Asn Leu His Lys Phe Pro Ile Val Leu Val 245 250 Gly Asn Lys Ser Asp Asp Thr His Arg Glu Val Ala Leu Asn Asp 265 270 260 Gly Ala Thr Cys Ala Met Glu Trp Asn Cys Ala Phe Met Glu Ile 280 275 285 Ser Ala Lys Thr Asp Val Asn Val Gln Glu Leu Phe His Met Leu 290 295 300 Leu Asn Tyr Lys Lys Pro Thr Thr Gly Leu Gln Glu Pro Glu 305 310 Lys Lys Ser Gln Met Pro Asn Thr Thr Glu Lys Leu Leu Asp Lys 320 325 330 Cys Ile Ile Met <210> 51 <211> 551 <212> PRT <213> Homo sapiens <220> <221> misc_feature <223> Incyte ID No: 2123286CD1 <400> 51 Met Glu Glu Leu Pro Leu Phe Ser Gly Asp Ser Gly Lys Pro 5 10 Val Gln Ala Thr Leu Ser Ser Leu Lys Met Leu Asp Val Gly Lys

```
Trp Pro Ile Phe Ser Leu Cys Ser Glu Glu Glu Leu Gln Leu Ile
                 35
                                      40
Arg Gln Ala Cys Val Phe Gly Ser Ala Gly Asn Glu Val Leu Tyr
                 50
Thr Thr Val Asn Asp Glu Ile Phe Val Leu Gly Thr Asn Cys Cys
                                      70
                 65
Gly Cys Leu Gly Leu Gly Asp Val Gln Ser Thr Ile Glu Pro Arg
                                                          90
                 80
                                      85
Arg Leu Asp Ser Leu Asn Gly Lys Lys Ile Ala Cys Leu Ser Tyr
                                     100
                 95
Gly Ser Gly Pro His Ile Val Leu Ala Thr Thr Glu Gly Glu Val
                                     115
                110
Phe Thr Trp Gly His Asn Ala Tyr Ser Gln Leu Gly Asn Gly Thr
                                     130
                125
Thr Asn His Gly Leu Val Pro Cys His Ile Ser Thr Asn Leu Ser
                140
                                     145
Asn Lys Gln Val Ile Glu Val Ala Cys Gly Ser Tyr His Ser Leu
                155
                                     160
Val Leu Thr Ser Asp Gly Glu Val Phe Ala Trp Gly Tyr Asn Asn
                                     175
                170
Ser Gly Gln Val Gly Ser Gly Ser Thr Val Asn Gln Pro Ile Pro
                                     190
                185
Arg Arg Val Thr Gly Cys Leu Gln Asn Lys Val Val Thr Ile
                                     205
                200
Ala Cys Gly Gln Met Cys Cys Met Ala Val Val Asp Thr Gly Glu
                                     220
                215
Val Tyr Val Trp Gly Tyr Asn Gly Asn Gly Gln Leu Gly Leu Gly
                230
                                     235
Asn Ser Gly Asn Gln Pro Thr Pro Cys Arg Val Ala Ala Leu Gln
                245
                                     250
Gly Ile Arg Val Gln Arg Val Ala Cys Gly Tyr Ala His Thr Leu
                                     265
                260
Val Leu Thr Asp Glu Gly Gln Val Tyr Ala Trp Gly Ala Asn Ser
                275
                                     280
Tyr Gly Gln Leu Gly Thr Gly Asn Lys Ser Asn Gln Ser Tyr Pro
                                     295
                290
Thr Pro Val Thr Val Glu Lys Asp Arg Ile Ile Glu Ile Ala Ala
                                     310
                305
Cys His Ser Thr His Thr Ser Ala Ala Lys Thr Gln Gly Gly His
                320
                                     325
Val Tyr Met Trp Gly Gln Cys Arg Gly Gln Ser Val Ile Leu Pro
                335
                                     340
His Leu Thr His Phe Ser Cys Thr Asp Asp Val Phe Ala Cys Phe
                                     355
                350
Ala Thr Pro Ala Val Thr Trp Arg Leu Leu Ser Val Glu Pro Asp
                                     370
                365
Asp His Leu Thr Val Ala Glu Ser Leu Lys Arg Glu Phe Asp Asn
                                     385
                380
Pro Asp Thr Ala Asp Leu Lys Phe Leu Val Asp Gly Lys Tyr Ile
                                     400
                395
Tyr Ala His Lys Val Leu Leu Lys Ile Arg Cys Glu His Phe Arg
                                     415
                410
Ser Ser Leu Glu Asp Asn Glu Asp Asp Ile Val Glu Met Ser Glu
                                     430
                425
Phe Ser Tyr Pro Val Tyr Arg Ala Phe Leu Glu Tyr Leu Tyr Thr
                                     445
                                                         450
                440
Asp Ser Ile Ser Leu Ser Pro Glu Glu Ala Val Gly Leu Leu Asp
                                     460
                455
Leu Ala Thr Phe Tyr Arg Glu Asn Arg Leu Lys Lys Leu Cys Gln
                470
                                     475
                                                         480
Gln Thr Ile Lys Gln Gly Ile Cys Glu Glu Asn Ala Ile Ala Leu
                                     490
```

```
Leu Ser Ala Ala Val Lys Tyr Asp Ala Gln Asp Leu Glu Glu Phe
                500
                                    505
Cys Phe Arg Phe Cys Ile Asn His Leu Thr Val Val Thr Gln Thr
                515
                                    520
Ser Gly Phe Ala Glu Met Asp His Asp Leu Leu Lys Asn Phe Ile
                530
                                    535
Ser Lys Ala Ser Arg Val Gly Ala Phe Lys Asn
                545
<210> 52
<211> 308
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2477507CD1
<400> 52
Met Ile His Asp Ala Gln Met Asp Tyr Tyr Gly Thr Arg Leu Ala
                                     10
Thr Cys Ser Ser Asp Arg Ser Val Lys Ile Phe Asp Val Arg Asn
Gly Gly Gln Ile Leu Ile Ala Asp Leu Arg Gly His Glu Gly Pro
Val Trp Gln Val Ala Trp Ala His Pro Met Tyr Gly Asn Ile Leu
                 50
                                     55
Ala Ser Cys Ser Tyr Asp Arg Lys Val Ile Ile Trp Arg Glu Glu
                 65
                                     70
Asn Gly Thr Trp Glu Lys Ser His Glu His Ala Gly His Asp Ser
                 80
                                     85
Ser Val Asn Ser Val Cys Trp Ala Pro His Asp Tyr Gly Leu Ile
                 95
                                    100
                                                        105
Leu Ala Cys Gly Ser Ser Asp Gly Ala Ile Ser Leu Leu Thr Tyr
                110
                                    115
                                                        120
Thr Gly Glu Gly Gln Trp Glu Val Lys Lys Ile Asn Asn Ala His
                125
Thr Ile Gly Cys Asn Ala Val Ser Trp Ala Pro Ala Val Val Pro
                                    145
                140
Gly Ser Leu Ile Asp His Pro Ser Gly Gln Lys Pro Asn Tyr Ile
                155
                                    160
Lys Arg Phe Ala Ser Gly Gly Cys Asp Asn Leu Ile Lys Leu Trp
                170
                                    175
Lys Glu Glu Glu Asp Gly Gln Trp Lys Glu Glu Gln Lys Leu Glu
                185
                                    190
Ala His Ser Asp Trp Val Arg Asp Val Ala Trp Ala Pro Ser Ile
                200
                                    205
                                                        210
Gly Leu Pro Thr Ser Thr Ile Ala Ser Cys Ser Gln Asp Gly Arg
                215
                                    220
Val Phe Ile Trp Thr Cys Asp Asp Ala Ser Ser Asn Thr Trp Ser
                230
                                    235
Pro Lys Leu Heu His Lys Phe Asn Asp Val Val Trp His Val Ser
                245
                                    250
Trp Ser Ile Thr Ala Asn Ile Leu Ala Val Ser Gly Gly Asp Asn
                260
                                    265
                                                        270
Lys Val Thr Leu Trp Lys Glu Ser Val Asp Gly Gln Trp Val Cys
                275
                                    280
                                                        285
Ile Ser Asp Val Asn Lys Gly Gln Gly Ser Val Ser Ala Ser Val
                290
                                    295 .
Thr Glu Gly Gln Gln Asn Glu Gln
                305
<210> 53
<211> 949
<212> PRT
```

<213> Homo sapiens <220> <221> misc_feature <223> Incyte ID No: 2759119CD1 <400> 53 Met Asp Ala Leu Glu Asp Tyr Val Trp Pro Arg Ala Thr Ser Glu Leu Ile Leu Leu Pro Val Thr Gly Leu Glu Cys Val Gly Asp Arg Leu Leu Ala Gly Glu Gly Pro Asp Val Leu Val Tyr Ser Leu Asp Phe Gly Gly His Leu Arg Met Ile Lys Arg Val Gln Asn Leu Leu Gly His Tyr Leu Ile His Gly Phe Arg Val Arg Pro Glu Pro Asn Gly Asp Leu Asp Leu Glu Ala Met Val Ala Val Phe Gly Ser Lys Gly Leu Arg Val Val Lys Ile Ser Trp Gly Gln Gly His Phe Trp Glu Leu Trp Arg Ser Gly Leu Trp Asn Met Ser Asp Trp Ile Trp Asp Ala Arg Trp Leu Glu Gly Asn Ile Ala Leu Ala Leu Gly His Asn Ser Val Val Leu Tyr Asp Pro Val Val Gly Cys Ile Leu Gln Glu Val Pro Cys Thr Asp Arg Cys Thr Leu Ser Ser Ala Cys Leu Ile Gly Asp Ala Trp Lys Glu Leu Thr Ile Val Ala Gly Ala Val Ser Asn Gln Leu Leu Val Trp Tyr Pro Ala Thr Ala Leu Ala Asp Asn Lys Pro Val Ala Pro Asp Arg Arg Ile Ser Gly His Val Gly Ile Ile Phe Ser Met Ser Tyr Leu Glu Ser Lys Gly Leu Leu Ala Thr Ala Ser Glu Asp Arg Ser Val Arg Ile Trp Lys Val Gly Asp Leu Arg Val Pro Gly Gly Arg Val Gln Asn Ile Gly His Cys Phe Gly His Ser Ala Arg Val Trp Gln Val Lys Leu Leu Glu Asn Tyr Leu Ile Ser Ala Gly Glu Asp Cys Val Cys Leu Val Trp Ser His Glu Gly Glu Ile Leu Gln Ala Phe Arg Gly His Gln Gly Arg Gly Ile Arg Ala Ile Ala Ala His Glu Arg Gln Ala Trp Val Ile Thr Gly Gly Asp Asp Ser Gly Ile Arg Leu Trp His Leu Val Gly Arg Gly Tyr Arg Gly Leu Gly Val Ser Ala Leu Cys Phe Lys Ser Arg Ser Arg Pro Gly Thr Leu Lys Ala Val Thr Leu Ala Gly Ser Trp Arg Leu Leu Ala Val Thr Asp Thr Gly Ala Leu Tyr Leu Tyr Asp Val Glu Val Lys Cys Trp Glu Gln Leu Leu Glu Asp Lys His Phe Gln Ser Tyr Cys Leu Leu Glu Ala Ala Pro Gly Pro Glu Gly Phe Gly Leu Cys Ala Met Ala Asn Gly Glu Gly Arg Val Lys Val Val

Pro Ile Asn Thr Pro Thr Ala Ala Val Asp Gln Thr Leu Phe Pro Gly Lys Val His Ser Leu Ser Trp Ala Leu Arg Gly Tyr Glu Glu Leu Leu Leu Leu Ala Ser Gly Pro Gly Gly Val Val Ala Cys Leu Glu Ile Ser Ala Ala Pro Ser Gly Lys Ala Ile Phe Val Lys Glu Arg Cys Arg Tyr Leu Leu Pro Pro Ser Lys Gln Arg Trp His Thr Cys Ser Ala Phe Leu Pro Pro Gly Asp Phe Leu Val Cys Gly Asp Arg Arg Gly Ser Val Leu Leu Phe Pro Ser Arg Pro Gly Leu Leu Lys Asp Pro Gly Val Gly Gly Lys Ala Arg Ala Gly Ala Gly Ala Pro Val Val Gly Ser Gly Ser Ser Gly Gly Gly Asn Ala Phe Thr Gly Leu Gly Pro Val Ser Thr Leu Pro Ser Leu His Gly Lys Gln Gly Val Thr Ser Val Thr Cys His Gly Gly Tyr Val Tyr Thr Ile Gly Arg Asp Gly Ala Tyr Tyr Gln Leu Phe Val Arg Asp Gly Gln Leu Gln Pro Val Leu Arg Gln Lys Ser Cys Arg Gly Met Asn Trp Leu Ala Gly Leu Arg Ile Val Pro Asp Gly Ser Met Val Ile Leu Gly Phe His Ala Asn Glu Phe Val Val Trp Asn Pro Arg Ser His Glu Lys Leu His Ile Val Asn Cys Gly Gly Gly His Arg Ser Trp Ala Phe Ser Asp Thr Glu Ala Ala Met Ala Phe Ala Tyr Leu Lys Asp Gly Asp Val Met Leu Tyr Arg Ala Leu Gly Gly Cys Thr Arg Pro His Val Ile Leu Arg Glu Gly Leu His Gly Arg Glu Ile Thr Cys Val Lys Arg Val Gly Thr Ile Thr Leu Gly Pro Glu Tyr Gly Val Pro Ser Phe Met Gln Pro Asp Asp Leu Glu Pro Gly Ser Glu Gly Pro Asp Leu Thr Asp Ile Val Ile Thr Cys Ser Glu Asp Thr Thr Val Cys Val Leu Ala Leu Pro Thr Thr Thr Gly Ser Ala His Ala Leu Thr Ala Val Cys Asn His Ile Ser Ser Val Arg Ala Val Ala Val Trp Gly Ile Gly Thr Pro Gly Gly Pro Gln Asp Pro Gln Pro Gly Leu Thr Ala His Val Val Ser Ala Gly Gly Arg Ala Glu Met His Cys Phe Ser Ile Met Val Thr Pro Asp Pro Ser Thr Pro Ser Arg Leu Ala Cys His Val Met His Leu Ser Ser His Arg Leu Asp Glu Tyr Trp Asp Arg Gln Arg Asn Arg His Arg Met Val Lys Val Asp Pro Glu Thr Arg Tyr Met Ser Leu Ala Val Cys Glu Leu Asp Gln Pro Gly Leu Gly Pro Leu Val Ala Ala Ala Cys Ser Asp Gly Ala Val Ser Ser Phe Phe Cys Arg Ile Leu Gly Gly Phe Cys

```
890
                                    895
Ser Ser Leu Leu Lys Pro Ser Thr Ile Ser Asp Val Ser Ser Arg
                                    910
                905
Ser Thr Pro Leu His Thr Arg His Pro Thr Arg Gly Gly Ser
                920
                                    925
Ser Cys Ala Ala Gln Leu Leu Met Ala Ala Trp Leu Ser Gly Ile
                                    940
                935
Ser Pro Pro Cys
<210> 54
<211> 227
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2823818CD1
<400> 54
Met Arg His Glu Ala Pro Met Gln Met Ala Ser Ala Gln Asp Ala
                                     10
Arg Tyr Gly Gln Lys Asp Ser Ser Asp Gln Asn Phe Asp Tyr Met
                 20
                                     25
Phe Lys Leu Leu Ile Ile Gly Asn Ser Ser Val Gly Lys Thr Ser
Phe Leu Phe Arg Tyr Ala Asp Asp Ser Phe Thr Ser Ala Phe Val
                                     55
                 50
Ser Thr Val Gly Ile Asp Phe Lys Val Lys Thr Val Phe Lys Asn
                 65
                                     70
Val Lys Arg Ile Lys Leu Gln Ile Trp Asp Thr Ala Gly Gln Glu
                                     85
                 80
Arg Tyr Arg Thr Ile Thr Thr Ala Tyr Tyr Arg Gly Ala Met Gly
                 95
                                    100
Phe Ile Leu Met Tyr Asp Ile Thr Asn Glu Glu Ser Phe Asn Ala
                110
                                    115
Val Gln Asp Trp Ser Thr Gln Ile Lys Thr Tyr Ser Trp Asp Asn
                                    130
                125
Ala Gln Val Ile Leu Val Gly Asn Lys Cys Asp Met Glu Asp Glu
                140
                                    145
Arg Val Ile Ser Thr Glu Arg Gly Gln His Leu Gly Glu Gln Leu
                                    160
                155
Gly Phe Glu Phe Phe Glu Thr Ser Ala Lys Asp Asn Ile Asn Val
                170
                                    175
                                                         180
Lys Gln Thr Phe Glu Arg Leu Val Asp Ile Ile Cys Asp Lys Met
                185
                                    190
Ser Glu Ser Leu Glu Thr Asp Pro Ala Ile Thr Ala Ala Lys Gln
                                    205
                                                         210
                200
Asn Thr Arg Leu Lys Glu Thr Pro Pro Pro Pro Gln Pro Asn Cys
                                    220
                                                         225
Ala Cys
<210> 55
<211> 474
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2859730CD1
<400> 55
Met Arg Arg Val Val Arg Gln Ser Lys Phe Arg His Val Phe Gly
                  5
```

```
Gln Ala Val Lys Asn Asp Gln Cys Tyr Asp Asp Ile Arg Val Ser
                 20
                                      25
Arg Val Thr Trp Asp Ser Ser Phe Cys Ala Val Asn Pro Arg Phe
                                      40
Val Ala Ile Ile Glu Ala Ser Gly Gly Gly Ala Phe Leu Val
                 50
                                     55
Leu Pro Leu Arg Lys Thr Gly Arg Ile Asp Lys Ser Tyr Pro Thr
                 65
                                     70
Val Cys Gly His Thr Gly Pro Val Leu Asp Ile Asp Trp Cys Pro
                                     85
                 80
His Asn Asp Gln Val Ile Ala Ser Gly Ser Glu Asp Cys Thr Val
                                     100
                 95
Met Val Trp Gln Ile Pro Glu Asn Gly Leu Thr Leu Ser Leu Thr
                110
                                     115
Glu Pro Val Val Ile Leu Glu Gly His Ser Lys Arg Val Gly Ile
                125
                                     130
                                                         135
Val Ala Trp His Pro Thr Ala Arg Asn Val Leu Leu Ser Ala Gly
                140
                                     145
                                                         150
Cys Asp Asn Ala Ile Ile Ile Trp Asn Val Gly Thr Gly Glu Ala
                155
                                     160
                                                         165
Leu Ile Asn Leu Asp Asp Met His Ser Asp Met Ile Tyr Asn Val
                170
                                     175
Ser Trp Asn Arg Asn Gly Ser Leu Ile Cys Thr Ala Ser Lys Asp
                185
                                     190
                                                         195
Lys Lys Val Arg Val Ile Asp Pro Arg Lys Gln Glu Ile Val Ala
                                     205
                200
Glu Lys Glu Lys Ala His Glu Gly Ala Arg Pro Met Arg Ala Ile
                215
                                     220
Phe Leu Ala Asp Gly Asn Val Phe Thr Thr Gly Phe Ser Arg Met
                230
                                     235
Ser Glu Arg Gln Leu Ala Leu Trp Asn Pro Lys Asn Met Gln Glu
                245
                                    250
                                                         255
Pro Ile Ala Leu His Glu Met Asp Thr Ser Asn Gly Val Leu Leu
                260
                                    265
                                                         270
Pro Phe Tyr Asp Pro Asp Thr Ser ile Ile Tyr Leu Cys Gly Lys
                275
                                     280
Gly Asp Ser Ser Ile Arg Tyr Phe Glu Ile Thr Asp Glu Ser Pro
                290
                                    295
Tyr Val His Tyr Leu Asn Thr Phe Ser Ser Lys Glu Pro Gln Arg
                305
                                    310
                                                         315
Gly Met Gly Tyr Met Pro Lys Arg Gly Leu Asp Val Asn Lys Cys
                320
                                    325
Glu Ile Ala Arg Phe Phe Lys Leu His Glu Arg Lys Cys Glu Pro
                335
                                    340
Ile Ile Met Thr Val Pro Arg Lys Ser Asp Leu Phe Gln Asp Asp
                350
                                    355
                                                         360
Leu Tyr Pro Asp Thr Ala Gly Pro Glu Ala Ala Leu Glu Ala Glu
                                    370
                365
Glu Trp Phe Glu Gly Lys Asn Ala Asp Pro Ile Leu Ile Ser Leu
                                    385
                380
Lys His Gly Tyr Ile Pro Gly Lys Asn Arg Asp Leu Lys Val Val
                395
                                    400
                                                         405
Lys Lys Asn Ile Leu Asp Ser Lys Pro Thr Ala Asn Lys Lys Cys
                410
                                    415
Asp Leu Ile Ser Ile Pro Lys Lys Thr Thr Asp Thr Ala Ser Val
                425
                                    430
                                                         435
Gln Asn Glu Ala Lys Leu Asp Glu Ile Leu Lys Glu Ile Lys Ser
                440
                                    445
Ile Lys Asp Thr Ile Cys Asn Gln Asp Glu Arg Ile Ser Lys Leu
                455
                                    460
Glu Gln Gln Met Ala Lys Ile Ala Ala
                470
```

<210> 56

```
<211> 547
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2861155CD1
<400> 56
Met Lys Thr Leu Glu Thr Gln Pro Leu Ala Pro Asp Cys Cys Pro
                                     10
Ser Asp Gln Asp Pro Ala Pro Ala His Pro Ser Pro His Ala Ser
                 20
                                     25
Pro Met Asn Lys Asn Ala Asp Ser Glu Leu Met Pro Pro Pro
                                     40
                 35
Glu Arg Gly Asp Pro Pro Arg Leu Ser Pro Asp Pro Val Ala Gly
                                     55
                 50
Ser Ala Val Ser Gln Glu Leu Arg Glu Gly Asp Pro Val Ser Leu
                                     70
                 65
Ser Thr Pro Leu Glu Thr Glu Phe Gly Ser Pro Ser Glu Leu Ser
                 80
                                     85
Pro Arg Ile Glu Glu Glu Leu Ser Glu Asn Thr Ser Leu Pro
                 95
                                    100
Ala Glu Glu Ala Asn Gly Ser Leu Ser Glu Glu Glu Ala Asn Gly
                                     115
Pro Glu Leu Gly Ser Gly Lys Ala Met Glu Asp Thr Ser Gly Glu
                125
                                    130
Pro Ala Ala Glu Asp Glu Gly Asp Thr Ala Trp Asn Tyr Ser Phe
                140
                                    145
Ser Gln Leu Pro Arg Phe Leu Ser Gly Ser Trp Ser Glu Phe Ser
                155
                                    160
Thr Gln Pro Glu Asn Phe Leu Lys Gly Cys Lys Trp Ala Pro Asp
                170
                                    175
Gly Ser Cys Ile Leu Thr Asn Ser Ala Asp Asn Ile Leu Arg Ile
                                    190
                185
Tyr Asn Leu Pro Pro Glu Leu Tyr His Glu Gly Glu Gln Val Glu
                200
                                    205
Tyr Ala Glu Met Val Pro Val Leu Arg Met Val Glu Gly Asp Thr
                215
                                    220
Ile Tyr Asp Tyr Cys Trp Tyr Ser Leu Met Ser Ser Ala Gln Pro
                230
                                    235
Asp Thr Ser Tyr Val Ala Ser Ser Ser Arg Glu Asn Pro Ile His
                245
                                    250
                                                         255
Ile Trp Asp Ala Phe Thr Gly Glu Leu Arg Ala Ser Phe Arg Ala
                260
                                    265
Tyr Asn His Leu Asp Glu Leu Thr Ala Ala His Ser Leu Cys Phe
                                    280
                                                         285
                275
Ser Pro Asp Gly Ser Gln Leu Phe Cys Gly Phe Asn Arg Thr Val
                290
                                    295
Arg Val Phe Ser Thr Ala Arg Pro Gly Arg Asp Cys Glu Val Arg
                305
                                    310
Ala Thr Phe Ala Lys Lys Gln Gly Gln Ser Gly Ile Ile Ser Cys
                320
                                    325
                                                         330
Ile Ala Phe Ser Pro Ala Gln Pro Leu Tyr Ala Cys Gly Ser Tyr
                335
                                    340
Gly Arg Ser Leu Gly Leu Tyr Ala Trp Asp Asp Gly Ser Pro Leu
                350
                                    355
Ala Leu Leu Gly Gly His Gln Gly Gly Ile Thr His Leu Cys Phe
                365
                                    370
His Pro Asp Gly Asn Arg Phe Phe Ser Gly Ala Arg Lys Asp Ala
                                                         390
                380
                                    385
Glu Leu Leu Cys Trp Asp Leu Arg Gln Ser Gly Tyr Pro Leu Trp
                395
                                    400
                                                         405
```

```
Ser Leu Gly Arg Glu Val Thr Thr Asn Gln Arg Ile Tyr Phe Asp
                410
                                     415
Leu Asp Pro Thr Gly Gln Phe Leu Val Ser Gly Ser Thr Ser Gly
                425
                                     430
Ala Val Ser Val Trp Asp Thr Asp Gly Pro Gly Asn Asp Gly Lys
                440
                                     445
                                                          450
Pro Glu Pro Val Leu Ser Phe Leu Pro Gln Lys Asp Cys Thr Asn
                455
                                     460
Gly Val Ser Leu His Pro Ser Leu Pro Leu Leu Ala Thr Ala Ser
                                                         480
                470
                                     475
Gly Gln Arg Val Phe Pro Glu Pro Thr Glu Ser Gly Asp Glu Gly
                485
                                     490
                                                         495
Glu Glu Leu Gly Leu Pro Leu Leu Ser Thr Arg His Val His Leu
                500
                                     505
Glu Cys Arg Leu Gln Leu Trp Trp Cys Gly Gly Pro Asp Ser
                515
                                     520
                                                         525
Ser Ile Pro Asp Asp His Gln Gly Glu Lys Gly Gln Gly Gly Thr
                530
                                     535
Gly Gly Arg Ser Trp Gly Ala
                545
<210> 57
<211> 686
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3002667CD1
<400> 57
Met Gly Glu Phe Lys Val His Arg Val Arg Phe Phe Asn Tyr Val
Pro Ser Gly Ile Arg Cys Val Ala Tyr Asn Asn Gln Ser Asn Arg
                                      25
                 20
Leu Ala Val Ser Arg Thr Asp Gly Thr Val Glu Ile Tyr Asn Leu
Ser Ala Asn Tyr Phe Gln Glu Lys Phe Phe Pro Gly His Glu Ser
                 50
                                      55
Arg Ala Thr Glu Ala Leu Cys Trp Ala Glu Gly Gln Arg Leu Phe
                 65
                                      70
Ser Ala Gly Leu Asn Gly Glu Ile Met Glu Tyr Asp Leu Gln Ala
                 80
                                      85
Leu Asn Ile Lys Tyr Ala Met Asp Ala Phe Gly Gly Pro Ile Trp
                 95
                                    100
                                                         105
Ser Met Ala Ala Ser Pro Ser Gly Ser Gln Leu Leu Val Gly Cys
                110
                                     115
                                                         120
Glu Asp Gly Ser Val Lys Leu Phe Gln Ile Thr Pro Asp Lys Ile
                125
                                     130
                                                         135
Gln Phe Glu Arg Asn Phe Asp Arg Gln Lys Ser Arg Ile Leu Ser
                140
                                     145
Leu Ser Trp His Pro Ser Gly Thr His Ile Ala Ala Gly Ser Ile
                155
                                     160
Asp Tyr Ile Ser Val Phe Asp Val Lys Ser Gly Ser Ala Val His
                170
                                    175
Lys Met Ile Val Asp Arg Gln Tyr Met Gly Val Ser Lys Arg Lys
                185
                                     190
                                                         195
Cys Ile Val Trp Gly Val Ala Phe Leu Ser Asp Gly Thr Ile Ile
                                                         210
                200
                                    205
Ser Val Asp Ser Ala Gly Lys Val Gln Phe Trp Asp Ser Ala Thr
                215
                                    220
Gly Thr Leu Val Lys Ser His Leu Ile Ala Asn Ala Asp Val Gln
                230
                                    235
Ser Ile Ala Val Ala Asp Gln Glu Asp Ser Phe Val Val Gly Thr
```

```
245
                                     250
Ala Glu Gly Thr Val Phe His Phe Gln Leu Val Pro Val Thr Ser
                260
                                     265
Asn Ser Ser Glu Lys Gln Trp Val Arg Thr Lys Pro Phe Gln His
                275
                                     280
His Thr His Asp Val Arg Thr Val Ala His Ser Pro Thr Ala Leu
                290
                                     295
Ile Ser Gly Gly Thr Asp Thr His Leu Val Phe Arg Pro Leu Met
                305
                                     310
Glu Lys Val Glu Val Lys Asn Tyr Asp Ala Ala Leu Arg Lys Ile
                320
                                     325
Thr Phe Pro His Arg Cys Leu Ile Ser Cys Ser Lys Lys Arg Gln
                335
                                     340
Leu Leu Leu Phe Gln Phe Ala His His Leu Glu Leu Trp Arg Leu
                350
                                     355
Gly Ser Thr Val Ala Thr Gly Lys Asn Gly Asp Thr Leu Pro Leu
                365
                                     370
Ser Lys Asn Ala Asp His Leu Leu His Leu Lys Thr Lys Gly Pro
                380
                                     385
                                                         390
Glu Asn Ile Ile Cys Ser Cys Ile Ser Pro Cys Gly Ser Trp Ile
                395
                                     400
                                                         405
Ala Tyr Ser Thr Val Ser Arg Phe Phe Leu Tyr Arg Leu Asn Tyr
                410
                                     415
                                                         420
Glu His Asp Asn Ile Ser Leu Lys Arg Val Ser Lys Met Pro Ala
                425
                                     130
Phe Leu Arg Ser Ala Leu Gln Ile Leu Phe Ser Glu Asp Ser Thr
                440
                                     445
Lys Leu Phe Val Ala Ser Asn Gln Gly Ala Leu His Ile Val Gln
                455
                                     460
Leu Ser Gly Gly Ser Phe Lys His Leu His Ala Phe Gln Pro Gln
                470
                                     475
                                                         480
Ser Gly Thr Val Glu Ala Met Cys Leu Leu Ala Val Ser Pro Asp
                485
                                     490
Gly Asn Trp Leu Ala Ala Ser Gly Thr Ser Ala Gly Val His Val
                500
                                     505
                                                         510
Tyr Asn Val Lys Gln Leu Lys Leu His Cys Thr Val Pro Ala Tyr
                515
                                    520
                                                         525
Asn Phe Pro Val Thr Ala Met Ala Ile Ala Pro Asn Thr Asn Asn
                530
                                    535
Leu Val Ile Ala His Ser Asp Gln Gln Val Phe Glu Tyr Ser Ile
                545
                                    550
Pro Asp Lys Gln Tyr Thr Asp Trp Ser Arg Thr Val Gln Lys Gln
                560
                                    565
                                                         570
Gly Phe His His Leu Trp Leu Gln Arg Asp Thr Pro Ile Thr His
                575
                                    580
Ile Ser Phe His Pro Lys Arg Pro Met His Ile Leu Leu His Asp
                590
                                    595
Ala Tyr Met Phe Cys Ile Ile Asp Lys Ser Leu Pro Leu Pro Asn
                605
                                    610
Asp Lys Thr Leu Leu Tyr Asn Pro Phe Pro Pro Thr Asn Glu Ser
                620
                                    625
Asp Val Ile Arg Arg Arg Thr Ala His Ala Phe Lys Ile Ser Lys
                635
                                    640
                                                         645
Ile Tyr Lys Pro Leu Leu Phe Met Asp Leu Leu Asp Glu Arg Thr
                650
                                    655
Leu Val Ala Val Glu Arg Pro Leu Asp Asp Ile Ile Ala Gln Leu
                665
                                    670
Pro Pro Pro Ile Lys Lys Lys Phe Gly Thr
                680
<210> 58
<211> 93
<212> PRT
```

<213> Homo sapiens

```
<220>
<221> misc_feature
<223> Incyte ID No: 3043734CD1
<400> 58
Met Thr Ser Lys Arg Lys Pro Cys Gln Thr Gln Leu Arg Arg Ser
                                     10
Ile Ser Glu Gln Leu Arg Asp Ser Thr Ala Arg Ala Trp Asp Leu
Leu Trp Lys Asn Val Arg Glu Arg Arg Leu Ala Glu Ile Glu Ala
                                     40
                                                          45
                 35
Lys Glu Ala Cys Asp Trp Leu Arg Ala Ala Gly Phe Pro Gln Tyr
                                                          60
Ala Gln Leu Tyr Glu Asp Ser Gln Phe Pro Ile Asn Ile Val Ala
                                     70
                 65
Val Lys Asn Asp His Asp Phe Leu Glu Lys Asp Leu Val Glu Pro
                                     85
Leu Cys Arg
<210> 59
<211> 521
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3294893CD1
<400> 59
Met Arg Arg Gly His Gly Gln Arg Arg Gly Gln Glu Ala Ile Leu
                                     10
Glu Ala His Asn Ser Lys Leu Pro Gly Ser Ile Gln His Val Tyr
                 20
                                     25
Gly Ala Gln His Pro Pro Phe Asp Pro Leu Leu His Gly Thr Leu
                                     40
                                                          45
Leu Arg Ser Thr Ala Lys Met Pro Thr Thr Pro Val Lys Ala Lys
                 50
                                     55
Arg Val Ser Thr Phe Gln Glu Phe Glu Ser Asn Thr Ser Asp Ala
                                     70
                 65
Trp Asp Ala Gly Glu Asp Asp Glu Leu Leu Ala Met Ala Ala
                 80
                                     85
Glu Ser Leu Asn Ser Glu Val Val Met Glu Thr Ala Asn Arg Val
                 95
                                    100
Leu Arg Asn His Ser Gln Arg Gln Gly Arg Pro Thr Leu Gln Glu
                                    115
                                                        120
                110
Gly Pro Gly Leu Gln Gln Lys Pro Arg Pro Glu Ala Glu Pro Pro
                125
                                    130
Ser Pro Pro Ser Gly Asp Leu Arg Leu Val Lys Ser Val Ser Glu
                                                        150
                                    145
                140
Ser His Thr Ser Cys Pro Ala Glu Ser Ala Ser Asp Ala Ala Pro
                155
                                    160
Leu Gln Arg Ser Gln Ser Leu Pro His Ser Ala Thr Val Thr Leu
                170
                                    175
Gly Gly Thr Ser Asp Pro Ser Thr Leu Ser Ser Ser Ala Leu Ser
                185
                                    190
                                                        195
Glu Arg Glu Ala Ser Arg Leu Asp Lys Phe Lys Gln Leu Leu Ala
                200
                                    205
Gly Pro Asn Thr Asp Leu Glu Glu Leu Arg Arg Leu Ser Trp Ser
                                    220
                215
Gly Ile Pro Lys Pro Val Arg Pro Met Thr Trp Lys Leu Leu Ser
                230
                                    235
Gly Tyr Leu Pro Ala Asn Val Asp Arg Pro Ala Thr Leu Gln
```

250

245

```
Arg Lys Gln Lys Glu Tyr Phe Ala Phe Ile Glu His Tyr Tyr Asp
                260
                                     265
Ser Arg Asn Asp Glu Val His Gln Asp Thr Tyr Arg Gln Ile His
                275
                                     280
                                                         285
Ile Asp Ile Pro Arg Met Ser Pro Glu Ala Leu Ile Leu Gln Pro
                290
                                     295
Lys Val Thr Glu Ile Phe Glu Arg Ile Leu Phe Ile Trp Ala Ile
                                                          315
                305
                                     310
Arg His Pro Ala Ser Gly Tyr Val Gln Gly Ile Asn Asp Leu Val
                320
                                     325
Thr Pro Phe Phe Val Val Phe Ile Cys Glu Tyr Ile Glu Ala Glu
                                     340
                335
Glu Val Asp Thr Val Asp Val Ser Gly Val Pro Ala Glu Val Leu
                350
                                     355
Cys Asn Ile Glu Ala Asp Thr Tyr Trp Cys Met Ser Lys Leu Leu
                                     370
                365
Asp Gly Ile Gln Asp Asn Tyr Thr Phe Ala Gln Pro Gly Ile Gln
                380
                                     385
                                                         390
Met Lys Val Lys Met Leu Glu Glu Leu Val Ser Arg Ile Asp Glu
                395
                                     400
Gln Val His Arg His Leu Asp Gln His Glu Val Arg Tyr Leu Gln
                410
                                     415
Phe Ala Phe Arg Trp Met Asn Asn Leu Leu Met Arg Glu Val Pro
                                     430
                                                          435
Leu Arg Cys Thr Ile Arg Leu Trp Asp Thr Tyr Gln Ser Glu Pro
                440
                                     445
Asp Gly Phe Ser His Phe His Leu Tyr Val Cys Ala Ala Phe Leu
                                     460
                455
Val Arg Trp Arg Lys Glu Ile Leu Glu Glu Lys Asp Phe Gln Glu
                470
                                     475
                                                          480
Leu Leu Phe Leu Gln Asn Leu Pro Thr Ala His Trp Asp Asp
                485
                                     490
Glu Asp Ile Ser Leu Leu Leu Ala Glu Ala Tyr Arg Leu Lys Phe
                                     505
                500
Ala Phe Ala Asp Ala Pro Asn His Tyr Lys Lys
                515
                                     520
<210> 60
<211> 751
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3349052CD1
<400> 60
Met Arg Leu Leu Gly Ala Ala Ala Val Ala Ala Leu Gly Arg Gly
Arg Ala Pro Ala Ser Leu Gly Trp Gln Arg Lys Gln Val Asn Trp
                                      25
Lys Ala Cys Arg Trp Ser Ser Ser Gly Val Ile Pro Asn Glu Lys
                                                          45
                 35
                                      40
Ile Arg Asn Ile Gly Ile Ser Ala His Ile Asp Ser Gly Lys Thr
                                      55
Thr Leu Thr Glu Arg Val Leu Tyr Tyr Thr Gly Arg Ile Ala Lys
                                      70
                 65
Met His Glu Val Lys Gly Lys Asp Gly Val Gly Ala Val Met Asp
                 80
                                      85
                                                          90
Ser Met Glu Leu Glu Arg Gln Arg Gly Ile Thr Ile Gln Ser Ala
                 95
                                     100
Ala Thr Tyr Thr Met Trp Lys Asp Val Asn Ile Asn Ile Ile Asp
                110
Thr Pro Gly His Val Asp Phe Thr Ile Glu Val Glu Arg Ala Leu
```

Arg	Val	Leu	Asp	125 Gly 140	Ala	Val	Leu	Val	130 Leu 145	Cys	Ala	Val	Gly	135 Gly 150.
Val	Gln	Cyś	Gln		Met	Thr	Val	Asn		Gln	Met	Lys	Arg	
Asn	Val	Pro	Phe	-	Thr	Phe	Ile	Asn		Leu	Asp	Arg	Met	Gly 180
Ser	Asn	Pro	Ala	Arg 185	Ala	Leu	Gln	Gln	Met 190	Arg	Ser	Lys	Leu	Asn 195
His	Asn	Ala	Ala	Phe 200	Met	Gln	Ile	Pro	Met 205	Gly	Leu	Glu	Gly	Asn 210
Phe	Lys	Gly	Ile	Ile 215	Asp	Leu	Ile	Glu	Glu 220	Arg	Ala	Ile	Tyr	Phe 225
_	_	_		230		Ile			235					240
				245		Thr			250				•	255
				260		Glu			265					270
	-			275		Ser	_		280					285
			_	290		Phe			295					300
	_			305		Gln			310					315
-				320		Glu		٠	325					330
_		_		335		Glu			340					345
	_	-		350		Pro Gln			355				_	360
		_		365		Asp			370					375
				380		Arg			385					390
_				395		Val			400					405
				410		Ser			415					420
	_			425		Glu			430					435
				440		Pro			445					450
Phe	Ser	Lys	Gly	455 Ile	Gly	Arg	Phe	Thr	460 Arg	Glu	Asp	Pro	Thr	465 Phe
Lys	Val	Tyr	Phe		Thr	Glu	Asn	Lys		Thr	Val	Ile	Ser	
Met	Gly	Glu	Leu		Leu	Glu	Ile	Tyr		Gln	Arg	Leu	Glu	
Glu	Tyr	Gly	Суѕ		Cys	Ile	Thr	Gly		Pro	Lys	Val	Ala	
Arg	Glu	Thr	Ile		Ala	Pro	Val	Pro		Asp	Phe	Thr	His	
Lys	Gln	Ser	Gly		Ala	Gly	Gln	туr		Lys	Val	Ile	Gly	
Leu	Glu	Pro	Leu		Pro	Glu	Asp	Tyr	550 Thr 565	Lys	Leu	Glu	Phe	
Asp	Glu	Thr	Phe	560 Gly 575	Ser	Asn	Ile	Pro		Gln	Phe	Val	Pro	570 Ala 585
Val	Glu	Lys	Gly		Leu	Asp	Ala	Cys		Lys	Gly	Pro	Leu	
				220										

```
Gly His Lys Leu Ser Gly Leu Arg Phe Val Leu Gln Asp Gly Ala
                                    610
                605
His His Met Val Asp Ser Asn Glu Ile Ser Phe Ile Arg Ala Gly
                                    625
                                                         630
                620
Glu Gly Ala Leu Lys Gln Ala Leu Ala Asn Ala Thr Leu Cys Ile
                                    640
                                                         645
                635
Leu Glu Pro Ile Met Ala Val Glu Val Val Ala Pro Asn Glu Phe
                650
                                    655
                                                         660
Gln Gly Gln Val Ile Ala Gly Ile Asn Arg Arg His Gly Val Ile
                                    670
                665
Thr Gly Gln Asp Gly Val Glu Asp Tyr Phe Thr Leu Tyr Ala Asp
                                    685
                680
Val Pro Leu Asn Asp Met Phe Gly Tyr Ser Thr Glu Leu Arg Ser
                                    700
                695
Cys Thr Glu Gly Lys Gly Glu Tyr Thr Met Glu Tyr Ser Arg Tyr
                                    715
                                                         720
                710
Gln Pro Cys Leu Pro Ser Thr Gln Glu Asp Val Ile Asn Lys Tyr
                725
                                     730
Leu Glu Ala Thr Gly Gln Leu Pro Val Lys Lys Gly Lys Ala Lys
                                    745
                740
Asn
<210> 61
<211> 666
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3357264CD1
<220>
<221> unsure
<222> 281
<223> unknown or other
<400> 61
Met Cys Gly Ala Val Ile Pro Leu His Lys Pro Ala Gly Arg Lys
                                     10
Leu Gln Asn Gln Arg Ala Ala Leu Asn Gln Gln Ile Leu Lys Ala
                                     25
                 20
Val Arg Met Arg Thr Gly Ala Glu Asn Leu Leu Lys Val Ala Thr
                 35
                                      40
                                                          45
Asn Ser Lys Val Arg Glu Gln Val Arg Leu Glu Leu Ser Phe Val
                 50
                                      55
Asn Ser Asp Leu Gln Met Leu Lys Glu Glu Leu Glu Gly Leu Asn
                                     70
                 65
Ile Ser Val Gly Val Tyr Gln Asn Thr Glu Glu Ala Phe Thr Ile
                                      85
                                                          90
                 80
Pro Leu Ile Pro Leu Gly Leu Lys Glu Thr Lys Asp Val Asp Phe
                 95
                                    100
Ala Val Val Leu Lys Asp Phe Ile Leu Glu His Tyr Ser Glu Asp
                                    115
                                                         120
                110
Gly Tyr Leu Tyr Glu Asp Glu Ile Ala Asp Leu Met Asp Leu Arg
                                    130
                125
Gln Ala Cys Arg Thr Pro Ser Arg Asp Glu Ala Gly Val Glu Leu
                                    145
                                                         150
                140
Leu Met Thr Tyr Phe Ile Gln Leu Gly Phe Val Glu Ser Arg Phe
                155
                                    160
Phe Pro Pro Thr Arg Gln Met Gly Leu Leu Phe Thr Trp Tyr Asp
                                                         180
                                    175
                170
Ser Leu Thr Gly Val Pro Val Ser Gln Gln Asn Leu Leu Glu
                                    190
```

```
Lys Ala Ser Val Leu Phe Asn Thr Gly Ala Leu Tyr Thr Gln Ile
                200
                                     205
Gly Thr Arg Cys Asp Arg Gln Thr Gln Ala Gly Leu Glu Ser Ala
                                     220
                                                          225
                215
Ile Asp Ala Phe Gln Arg Ala Ala Gly Val Leu Asn Tyr Leu Lys
                                     235
                                                          240
                230
Asp Thr Phe Thr His Thr Pro Ser Tyr Asp Met Ser Pro Ala Met
                245
                                     250
Leu Ser Val Leu Val Lys Met Met Leu Ala Gln Ala Gln Glu Ser
                                                          270
                                     265
                260
Val Phe Glu Lys Ile Ser Leu Pro Gly Ile Xaa Asn Glu Phe Phe
                                     280
                275
Met Leu Val Lys Val Ala Gln Glu Ala Ala Lys Val Gly Glu Val
                                     295
                290
Tyr Gln Gln Leu His Ala Ala Met Ser Gln Ala Pro Val Lys Glu
                305
                                     310
                                                          315
Asn Ile Pro Tyr Ser Trp Ala Ser Leu Ala Cys Val Lys Ala His
                320
                                     325
His Tyr Ala Ala Leu Ala His Tyr Phe Thr Ala Ile Leu Leu Ile
                                                          345
                335
                                     340
Asp His Gln Val Lys Pro Gly Thr Asp Leu Asp His Gln Glu Lys
                                     355
                350
Cys Leu Ser Gln Leu Tyr Asp His Met Pro Glu Gly Leu Thr Pro
                                     370
                365
Leu Ala Thr Leu Lys Asn Asp Gln Gln Arg Arg Gln Leu Gly Lys
                380
                                     385
                                                          390
Ser His Leu Arg Arg Ala Met Ala His His Glu Glu Ser Val Arg
                395
                                     400
                                                          405
Glu Ala Ser Leu Cys Lys Lys Leu Arg Thr Ile Glu Val Leu Gln
                                     415
                410
                                                          420
Lys Val Leu Cys Ala Ala Gln Glu Arg Ser Arg Leu Thr Tyr Ala
                                     430
                                                          435
                425
Gln His Gln Glu Glu Asp Asp Leu Leu Asn Leu Ile Asp Ala Pro
                440
                                     445
Ser Val Val Ala Lys Thr Glu Gln Glu Val Asp Ile Ile Leu Pro
                                     460
                                                          465
                455
Gln Phe Ser Lys Leu Thr Val Thr Asp Phe Phe Gln Lys Leu Gly
                470
                                     475
Pro Leu Ser Val Phe Ser Ala Asn Lys Arg Trp Thr Pro Pro Arg
                485
                                     490
                                                          495
Ser Ile Arg Phe Thr Ala Glu Glu Gly Asp Leu Gly Phe Thr Leu
                500
                                     505
Arg Gly Asn Ala Pro Val Gln Val His Phe Leu Asp Pro Tyr Cys
                                     520
                                                          525
                515
Ser Ala Ser Val Ala Gly Ala Arg Glu Gly Asp Tyr Ile Val Ser
                530
                                     535
                                                          540
Ile Gln Leu Val Asp Cys Lys Trp Leu Thr Leu Ser Glu Val Met
                                                          555
                545
                                     550
Lys Leu Leu Lys Ser Phe Gly Glu Asp Glu Ile Glu Met Lys Val
                560
                                     565
                                                          570
Val Ser Leu Leu Asp Ser Thr Ser Ser Met His Asn Lys Ser Ala
                575
                                     580
Thr Tyr Ser Val Gly Met Gln Lys Thr Tyr Ser Met Ile Cys Leu
                590
                                     595
Ala Ile Asp Asp Asp Asp Lys Thr Asp Lys Thr Lys Lys Ile Ser
                605
                                     610
                                                          615
Lys Lys Leu Ser Phe Leu Ser Trp Gly Thr Asn Lys Asn Arg Gln
                                     625
                620
                                                          630
Lys Ser Ala Ser Thr Leu Cys Leu Pro Ser Val Gly Ala Ala Arg
                635
                                     640
                                                          645
Pro Gln Val Lys Lys Leu Pro Ser Pro Phe Ser Leu Leu Asn
                650
Ser Asp Ser Ser Trp Tyr
```

<210> 62 <211> 746

<212> PRT

<213> Homo sapiens

<220>

<221> misc_feature

<223> Incyte ID No: 3576329CD1

<400> 62 Met Ala Gly Ser Arg Gly Ala Gly Arg Thr Ala Ala Pro Ser Val Arg Pro Glu Lys Arg Arg Ser Glu Pro Glu Leu Glu Pro Glu Pro Glu Pro Glu Pro Pro Leu Leu Cys Thr Ser Pro Leu Ser His Ser Thr Gly Ser Asp Ser Gly Val Ser Asp Ser Glu Glu Ser Val Phe Ser Gly Leu Glu Asp Ser Gly Ser Asp Ser Ser Glu Asp Asp Asp Glu Gly Asp Glu Glu Gly Glu Asp Gly Ala Leu Asp Asp Glu Gly His Ser Gly Ile Lys Lys Thr Thr Glu Glu Gln Val Gln Ala Ser Thr Pro Cys Pro Arg Thr Glu Met Ala Ser Ala Arg Ile Gly Asp Glu Tyr Ala Glu Asp Ser Ser Asp Glu Glu Asp Ile Arg Asn Thr Val Gly Asn Val Pro Leu Glu Trp Tyr Asp Asp Phe Pro His Val Gly Tyr Asp Leu Asp Gly Arg Arg Ile Tyr Lys Pro Leu Arg Thr Arg Asp Glu Leu Asp Gln Phe Leu Asp Lys Met Asp Asp Pro Asp Tyr Trp Arg Thr Val Gln Asp Pro Met Thr Gly Arg Asp Leu Arg Leu Thr Asp Glu Gln Val Ala Leu Val Arg Arg Leu Gln Ser Gly Gln Phe Gly Asp Val Gly Phe Asn Pro Tyr Glu Pro Ala Val Asp Phe Phe Ser Gly Asp Val Met Ile His Pro Val Thr Asn Arg Pro Ala Asp Lys Arg Ser Phe Ile Pro Ser Leu Val Glu Lys Glu Lys Val Ser Arg Met Val His Ala Ile Lys Met Gly Trp Ile Gln Pro Arg Arg Pro Arg Asp Pro Thr Pro Ser Phe Tyr Asp Leu Trp Ala Gln Glu Asp Pro Asn Ala Val Leu Gly Arg His Lys Met His Val Pro Ala Pro Lys Leu Ala Leu Pro Gly His Ala Glu Ser Tyr Asn Pro Pro Pro Glu Tyr Leu Leu Ser, Glu Glu Glu Arg Leu Ala Trp Glu Gln Gln Glu Pro Gly Glu Arg Lys Leu Gly Phe Leu Pro Arg Lys Phe Pro Ser Leu Arg Ala Val Pro Ala Tyr Gly Arg Phe Ile Gln Glu Arg Phe Glu Arg Cys Leu Asp Leu Tyr Leu Cys Pro Arg Gln Arg Lys Met Arg Val Asn Val Asp Pro Glu Asp Leu Ile Pro

```
Lys Leu Pro Arg Pro Arg Asp Leu Gln Pro Phe Pro Thr Cys Gln
                395
                                    400
Ala Leu Val Tyr Arg Gly His Ser Asp Leu Val Arg Cys Leu Ser
                410
                                    415
                                                         420
Val Ser Pro Gly Gly Gln Trp Leu Val Ser Gly Ser Asp Asp Gly
                                    430
                                                         435
                425
Ser Leu Arg Leu Trp Glu Val Ala Thr Ala Arg Cys Val Arg Thr
                440
                                    445
                                                         450
Val Pro Val Gly Gly Val Val Lys Ser Val Ala Trp Asn Pro Ser
                455
                                    460
Pro Ala Val Cys Leu Val Ala Ala Ala Val Glu Asp Ser Val Leu
                                    475
                470
Leu Leu Asn Pro Ala Leu Gly Asp Arg Leu Val Ala Gly Ser Thr
                                    490
                485
Asp Gln Leu Leu Ser Ala Phe Val Pro Pro Glu Glu Pro Pro Leu
                                    505
                500
Gln Pro Ala Arg Trp Leu Glu Ala Ser Glu Glu Glu Arg Gln Val
                515
                                    520
Gly Leu Arg Leu Arg Ile Cys His Gly Lys Pro Val Thr Gln Val
                                    535
                                                         540
                530
Thr Trp His Gly Arg Gly Asp Tyr Leu Ala Val Val Leu Ala Thr
                545
                                    550
Gln Gly His Thr Gln Val Leu Ile His Gln Leu Ser Arg Arg
                560
                                    565
Ser Gln Ser Pro Phe Arg Arg Ser His Gly Gln Val Gln Arg Val
                                    580
                575
Ala Phe His Pro Ala Arg Pro Phe Leu Leu Val Ala Ser Gln Arg
                                    595
                590
Ser Val Arg Leu Tyr His Leu Leu Arg Gln Glu Leu Thr Lys Lys
                605
                                    610
Leu Met Pro Asn Cys Lys Trp Val Ser Ser Leu Ala Val His Pro
                620
                                    625
                                                         630
Ala Gly Asp Asn Val Ile Cys Gly Ser Tyr Asp Ser Lys Leu Val
                635
                                    640
                                                         645
Trp Phe Asp Leu Asp Leu Ser Thr Lys Pro Tyr Arg Met Leu Arg
                                    655
                650
                                                         660
His His Lys Lys Ala Leu Arg Ala Val Ala Phe His Pro Arg Tyr
                                    670
                                                         675
                665
Pro Leu Phe Ala Ser Gly Ser Asp Asp Gly Ser Val Ile Val Cys
                                    685
                680
                                                         690
His Gly Met Val Tyr Asn Asp Leu Leu Gln Asn Pro Leu Leu Val
                695
                                    700
                                                         705
Pro Val Lys Val Leu Lys Gly His Val Leu Thr Arg Asp Leu Gly
                710
                                    715
Val Leu Asp Val Ile Phe His Pro Thr Gln Pro Trp Val Phe Ser
                                    730
                725
Ser Gly Ala Asp Gly Thr Val Arg Leu Phe Thr
<210> 63
<211> 212
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3805550CD1
<400> 63
Met Ala Gly Pro Gly Pro Gly Pro Gly Asp Pro Asp Glu Gln Tyr
                                     10
                                                         15
Asp Phe Leu Phe Lys Leu Val Leu Val Gly Asp Ala Ser Val Gly
```

Lys Thr Cys Val Val Gln Arg Phe Lys Thr Gly Ala Phe Ser Glu

```
Arg Gln Gly Ser Thr Ile Gly Val Asp Phe Thr Met Lys Thr Leu
                 50
                                     55
Glu Ile Gln Gly Lys Arg Val Lys Leu Gln Ile Trp Asp Thr Ala
                                     70
Gly Gln Glu Arg Phe Arg Thr Ile Thr Gln Ser Tyr Tyr Arg Ser
                 80
                                     85
Ala Asn Gly Ala Ile Leu Ala Tyr Asp Ile Thr Lys Arg Ser Ser
                 95
                                    100
Phe Leu Ser Val Pro His Trp Ile Glu Asp Val Arg Lys Tyr Ala
                110
                                    115
Gly Ser Asn Ile Val Gln Leu Leu Ile Gly Asn Lys Ser Asp Leu
                125
                                    130
Ser Glu Leu Arg Glu Val Ser Leu Ala Glu Ala Gln Ser Leu Ala
                140
                                    145
Glu His Tyr Asp Ile Leu Cys Ala Ile Glu Thr Ser Ala Lys Asp
                                    160
                155
Ser Ser Asn Val Glu Glu Ala Phe Leu Arg Val Ala Thr Glu Leu
                170
                                    175
Ile Met Arg His Gly Gly Pro Leu Phe Ser Glu Lys Ser Pro Asp
               185
                                    190
His Ile Gln Leu Asn Ser Lys Asp Ile Gly Glu Gly Trp Gly Cys
                200
                                    205
                                                         210
Gly Cys
<210> 64
<211> 307
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 4546403CD1
<400> 64
Met Arg Cys Leu His Ser Glu Lys Ala His Asp Leu Gly Ile Thr
Cys Cys Asp Phe Ser Ser Gln Pro Val Ser Asp Gly Glu Gln Gly
Leu Gln Phe Phe Arg Leu Ala Ser Cys Gly Gln Asp Cys Gln Val
                 35
                                     40
Lys Ile Trp Ile Val Ser Phe Thr His Ile Leu Gly Phe Glu Leu
                                     55
                 50
Lys Tyr Lys Ser Thr Leu Ser Gly His Cys Ala Pro Val Leu Ala
                                     70
                 65
Cys Ala Phe Ser His Asp Gly Gln Met Leu Val Ser Gly Ser Val
                80
                                     85
Asp Lys Ser Val Ile Val Tyr Asp Thr Asn Thr Glu Asn Ile Leu
His Thr Leu Thr Gln His Thr Arg Tyr Val Thr Thr Cys Ala Phe
                                    115
                110
Ala Pro Asn Thr Leu Leu Leu Ala Thr Gly Ser Met Asp Lys Thr
                125
                                    130
Val Asn Ile Trp Gln Phe Asp Leu Glu Thr Leu Cys Gln Ala Arg
                140
                                    145
Ser Thr Glu His Gln Leu Lys Gln Phe Thr Glu Asp Trp Ser Glu
                155
                                    160
                                                        165
Glu Asp Val Ser Thr Trp Leu Cys Ala Gln Asp Leu Lys Asp Leu
                170
                                    175
Val Gly Ile Phe Lys Met Asn Asn Ile Asp Gly Lys Glu Leu Leu
               185
                                    190
Asn Leu Thr Lys Glu Ser Leu Ala Asp Asp Leu Lys Ile Glu Ser
                                    205
```

```
Leu Gly Leu Arg Ser Lys Val Leu Arg Lys Ile Glu Glu Leu Arg
                215
                                    220
Thr Lys Val Lys Ser Leu Ser Ser Gly Ile Pro Asp Glu Phe Ile
                230
                                    235
Cys Pro Ile Thr Arg Glu Leu Met Lys Asp Pro Val Ile Ala Ser
                                    250
                245
                                                         255
Asp Gly Tyr Ser Tyr Glu Lys Glu Ala Met Glu Asn Trp Ile Ser
                260
                                    265
Lys Lys Lys Arg Thr Ser Pro Met Thr Asn Leu Val Leu Pro Ser
                275
                                    280
Ala Val Leu Thr Pro Asn Arg Thr Leu Lys Met Ala Ile Asn Arg
                290
                                    295
Trp Leu Glu Thr His Gln Lys
                305
<210> 65
<211> 378
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 4767318CD1
<400> 65
Met Arg Ala Ala Ala Pro Gly Leu Thr Ala Pro Trp Arg Leu
                                     10
Leu Gln Cys Cys Glu Leu Glu Ala Gly Glu Leu Gly Met Ala Val
                 20
                                     25
Pro Ala Ala Ala Met Gly Pro Ser Ala Leu Gly Gln Ser Gly Pro
                                     40
                 35
Gly Ser Met Ala Pro Trp Cys Ser Val Ser Ser Gly Pro Ser Arg
                 50
                                     55
Tyr Val Leu Gly Met Gln Glu Leu Phe Arg Gly His Ser Lys Thr
                 65
                                     70
Arg Glu Phe Leu Ala His Ser Ala Lys Val His Ser Val Ala Trp
                                     85
Ser Cys Asp Gly Arg Arg Leu Ala Ser Gly Ser Phe Asp Lys Thr
                 95
                                    100
Ala Ser Val Phe Leu Leu Glu Lys Asp Arg Leu Val Lys Glu Asn
                110
                                    115
Asn Tyr Arg Gly His Gly Asp Ser Val Asp Gln Leu Cys Trp His
                125
                                    130
                                                        135
Pro Ser Asn Pro Asp Leu Phe Val Thr Ala Ser Gly Asp Lys Thr
                140
                                    145
Ile Arg Ile Trp Asp Val Arg Thr Thr Lys Cys Ile Ala Thr Val
                155
                                    160
Asn Thr Lys Gly Glu Asn Ile Asn Ile Cys Trp Ser Pro Asp Gly
                170
                                    175
Gln Thr Ile Ala Val Gly Asn Lys Asp Asp Val Val Thr Phe Ile
                185
                                    190
Asp Ala Lys Thr His Arg Ser Lys Ala Glu Glu Gln Phe Lys Phe
                200
                                    205
Glu Val Asn Glu Ile Ser Trp Asn Asn Asp Asn Asn Met Phe Phe
                215
                                    220
Leu Thr Asn Gly Asn Gly Cys Ile Asn Ile Leu Ser Tyr Pro Glu
                230
                                    235
Leu Lys Pro Val Gln Ser Ile Asn Ala His Pro Ser Asn Cys Ile
                245
                                    250
Cys Ile Lys Phe Asp Pro Met Gly Lys Tyr Phe Ala Thr Gly Ser
                260
                                    265
                                                        270
Ala Asp Ala Leu Val Ser Leu Trp Asp Val Asp Glu Leu Val Cys
                                    280
Val Arg Cys Phe Ser Arg Leu Asp Trp Pro Val Arg Thr Leu Ser
```

```
290
                                    295
Phe Ser His Asp Gly Lys Met Leu Ala Ser Ala Ser Glu Asp His
                305
                                     310
Phe Ile Asp Ile Ala Glu Val Glu Thr Gly Asp Lys Leu Trp Glu
                                     325
                320
                                                         330
Val Gln Cys Glu Ser Pro Thr Phe Thr Val Ala Trp His Pro Lys
                                     340
                335
Arg Pro Leu Leu Ala Phe Ala Cys Asp Asp Lys Asp Gly Lys Tyr
                                     355
                350
                                                         360
Asp Ser Ser Arg Glu Ala Gly Thr Val Lys Leu Phe Gly Leu Pro
                                     370
Asn Asp Ser
<210> 66
<211> 466
<212> PRT
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 4834527CD1
<400> 66
Met Pro Gln Thr Leu Ser Ala Ser Asp Met Val Thr Pro Gly Ser
 1
Leu Ser Pro Pro Pro Thr Glu Pro Thr Asp Gly Glu Gln Ala Gly
                                      25
                 20
Gln Pro Leu Leu Asp Gly Ala Pro Ser Ser Ala Ser Leu Glu Thr
                 35
                                     40
Leu Ile Gln His Leu Val Pro Thr Ala Asp Tyr Tyr Pro Glu Lys
                 50
                                     55
Ala Tyr Ile Phe Thr Phe Leu Leu Ser Ser Arg Leu Phe Ile Glu
                                     70
                 65
Pro Arg Glu Leu Leu Ala Arg Val Cys His Leu Cys Ile Glu Gln
                                     85
Gln Gln Leu Asp Lys Pro Val Leu Asp Lys Ala Arg Val Arg Lys
                 95
                                    100
                                                         105
Phe Gly Pro Lys Leu Leu Gln Leu Leu Ala Glu Trp Thr Glu Thr
                110
                                    115
Phe Pro Arg Asp Phe Gln Glu Glu Ser Thr Ile Gly His Leu Lys
                125
                                    130
                                                         135
Asp Val Val Gly Arg Ile Ala Pro Cys Asp Glu Ala Tyr Arg Lys
                                    145
                140
                                                         150
Arg Met His Gln Leu Leu Gln Ala Leu His Gln Lys Leu Ala Ala
                155
                                    160
Leu Arg Gln Gly Pro Glu Gly Leu Val Gly Ala Asp Lys Pro Ile
                170
                                    175
                                                         180
Ser Tyr Arg Thr Lys Pro Pro Ala Ser Ile His Arg Glu Leu Leu
                185
                                    190
                                                         195
Gly Val Cys Ser Asp Pro Tyr Thr Leu Ala Gln Gln Leu Thr His
                200
                                    205
Val Glu Leu Glu Arg Leu Arg His Ile Gly Pro Glu Glu Phe Val
                215
                                    220
                                                         225
Gln Ala Phe Val Asn Lys Asp Pro Leu Ala Ser Thr Lys Pro Cys
                230
                                    235
                                                         240
Phe Ser Asp Lys Thr Ser Asn Leu Glu Ala Tyr Val Lys Trp Phe
                245
                                    250
                                                         255
Asn Arg Leu Cys Tyr Leu Val Ala Thr Glu Ile Cys Met Pro Ala
                260
                                    265
                                                         270
Lys Lys Lys Gln Arg Ala Gln Val Ile Glu Phe Phe Ile Asp Val
                275
                                                         285
                                    280
Ala Arg Glu Cys Phe Asn Ile Gly Asn Phe Asn Ser Leu Met Ala
                290
                                    295
                                                         300
```

```
Ile Ile Ser Gly Met Asn Met Ser Pro Val Ser Arg Leu Lys Lys
                                    310
                305
Thr Trp Ala Lys Val Arg Thr Ala Lys Phe Phe Ile Leu Glu His
                                    325
                                                         330
                320
Gln Met Asp Pro Thr Gly Asn Phe Cys Asn Tyr Arg Thr Ala Leu
                                    340
                                                         345
                335
Arg Gly Ala Ala His Arg Ser Leu Thr Ala His Ser Ser Arg Glu
                350
                                    355
                                                         360
Lys Ile Val Ile Pro Phe Phe Ser Leu Leu Ile Lys Asp Ile Tyr
                                    370
                                                         375
                365
Phe Leu Asn Glu Gly Cys Ala Asn Arg Leu Pro Asn Gly His Val
                                    385
                                                         390
                380
Asn Phe Glu Lys Phe Leu Glu Leu Ala Lys Gln Val Gly Glu Phe
                                     400
                395
Ile Thr Trp Lys Gln Val Glu Cys Pro Phe Glu Gln Asp Ala Ser
                410
                                     415
                                                         420
Ile Thr His Tyr Leu Tyr Thr Ala Pro Ile Phe Ser Glu Asp Gly
                425
                                    430
                                                         435
Leu Tyr Leu Ala Ser Tyr Glu Ser Glu Ser Pro Glu Asn Gln Thr
                                                         450
                                    445
                440
Glu Lys Glu Arg Trp Lys Ala Leu Arg Ser Ser Ile Leu Gly Lys
                455
                                    460
                                                         465
Thr
<210> 67
<211> 891
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1405545CB1
ggagaatggc ggcgccgggc tgcggctggg agcgggaaga ctctttgaaa tgcctgcggt 60
gctagagcga ctgagccgct ataatagcac gtcccaagct tttgctgagg tgctgcggct 120
gccgaagcag cagctgagga agctgctgta cccgctgcag gaagtagagc ggttcctcgc 180
cccctacggg aggcaagacc ttcacctgcg tatctttgac ccaagcccgg aggacatagc 240
cagggeggac aacatettea eggecaetga aeggaacege ategaetaeg teageteege 300
cgtccgtatc gaccacgccc cggaccttcc gcggccagag gtgtgtttta taggcagaag 360
caatgttgga aaatcatctc taatcaaggc tttattttca ctggcccctg aggttgaagt 420
cagagtetee aaaaaaccag gacacacaaa gaaaatgaat tttttcaaag ttggaaaaca 480
ttttacagtg gtggacatgc caggttatgg ctttagagca cctgaagatt ttgttgacat 540
ggtagagacc tatctaaaag aacgaaggaa cttgaagaga acatttttat tagtggatag 600
cgttgttgga attcaaaaaa cagacaatat tgccatagaa atgtgtgaag aatttgcatt 660
accttatgtg attgtattaa caaaaattga caaatcttcc aagggacatc ttttaaaaca 720
agtgcttcag atccagaaat ttgttaacat gaaaactcaa ggatgttttc ctcagttgtt 780
tcctgtaagt gctgtgacet tttctggaat ccacctgttg agatgcttta tagccagtgt 840
aacaggaagt cttgactaat ggttcccggt ttagctgaag attcaaaaaa a
                                                                   891
<210> 68
<211> 1512
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1451265CB1
<400> 68
gcccatggag gtggccgtgt gtacggactc ggcggccccg atgtggagct gcatcgtgtg 60
ggaacttcac tegggegeca acetgeteac etacegegge ggccaggegg gacccegegg 120
cctggcgctg ctcaatggcg agtatctgct ggcggcgcag ctgggcaaga attacatcag 180
```

```
cgcctgggag ctccagcgga aggaccagct ccagcagaag atcatgtgcc ccqqqcctgt 240
cacctgtctg actgcatcac ccaatggtct ctacgtcctg gcaggagttg cagaaagcat 300
ccacctgtgg gaggtctcca ccgggaacct tctggtcatc ctgagtcgac actaccagga 360
cgtctcctgc cttcagttca caggggacag cagccacttc atctcagggg gcaaggactg 420
cctggtgctg gtttggagcc tctgcagcgt gctgcaggcc gacccctcca ggattccggc 480
gcccaggcac gtctggtctc accacacgct ccccatcacg gacctgcact gcggctttgg 540
gggcccctg gcccgggtgg ccacttctc actggaccag acggtgaagc tatqqqaggt 600
ctectegggg gagetgetge teteegteet etttgaegtg tecateatgg eagtgaeeat 660
ggacetgget gagcaccata tgttctgcgg gggcagtgag ggctccatct tccaggtcga 720
cctcttcacc tggcccggac agagggagag gagcttccac ccagagcagg acgccgggaa 780
ggtcttcaaa gggcacagga accaggtgac ttgcctgtca gtgtccactg acggcagcgt 840
gctgctctca ggctcccacg acgagaccgt gcgcctctgg gacgtgcaga gcaagcagtg 900
cateeggacg gtggccetca aaggeceagt caccaatgee gccateetge tggegeeegt 960
cagcatgctg agetcagact tcaggcccag cctgccgctg ccccacttca acaagcacct 1020
gctgggcgcc gagcacgggg acgagccgcg ccacgggggc ctcactctgc gcctgggcct 1080
ccaccageag ggctcggagc ccagctacct ggaccgcacg gagcagctgc aggccgtcct 1140
gtgcagcacc atggagaaga gcgtgctcgg cggccaggac cagctgcgcg tccgtgtgac 1200
ggagctggag gacgaggtgc gcaacctgcg caagatcaat cgggacctgt tcgacttctc 1260
cacgcgcttc atcacgcggc cggccaagtg aggcccggag accccggccc gaggcgccca 1320
ggcctgagcc ccatgcctcc cagcaaccag ggcccgcggg tgtggccccc accagcccag 1380
geotogacte tecteagtte totgtegtgt tegggttttt cetetgtgae toggeegtet 1440
tggtgtctcg tggcacgcgt cacagtggtg ctagtctgtt tttaacaaaa qaggatgaaa 1500
aaaaaaaaa aa
                                                                     1512
<210> 69
<211> 2536
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1556311CB1
<400> 69
caactettgt tgaagetttt aggegtegea gactetteat ttgtgaggge gaceteteee 60
gaggggctct tttcacacaa atatccccac ggcgtttctc ggaggcaccc ccgtcatacg 120
tettgtetet egegacaatt etetttgaag gegaggeatt teaccacaac tetttteaac 180 caacetggeg acaacacca gagettacat tgaceccaat ttgaattte ateggeecaa 240
ggctttcttt acactcaggg aactctcaca ctccttaggg ggaaaaaggc ttcgttaagg 300
gccttgcaag ggttaccggg ttccggaatt ttcccggggg cccctcggct ggccaggact 360
gaaacccaga cgagcatgcc agaaacagtc aaccataaca aacatgggaa cgtagctctc 420
cctggaacga aaccaactcc catccctcca ccccggctga agaagcaggc ttcttttctg 480
gaagcagagg gcggtgcaaa gaccttgagc ggcggccggc cgggcgcagg cccggagctg 540
gagetgggca cagetggcag cccaggtggg geeeegeetg aggeegeee gggggattge 600
acaagggccc cgccgcccag ctctgaatca cggcccccgt gccatggagg ccggcagcgg 660
ctgagcgaca tgagcatttc tacttectec tecgactege tggagttega eeggagcatg 720
cetetgtttg getacgagge ggacaccaac ageageetgg aggactacga gggggaaagt 780
gaccaagaga ccatggcgcc ccccatcaag tccaaaaaga aaaggagcag ctccttcgtg 840
ctgcccaage tegtcaagte ccagetgeag aaggtgageg gggtgtteag eteetteatg 900 acceeggaga ageggatggt cegeaggate geegagettt eeegggacaa atgeacetae 960
ttcgggtgct tagtgcagga ctacgtgagc ttcctgcagg agaacaagga gtgccacgtg 1020
tccagcaccg acatgctgca gaccatccgg cagttcatga cccaggtcaa gaactatttg 1080
teteagaget eggagetgga ecceecate gagtegetga teeetgaaga ecaaatagat 1140
gtggtgctgg aaaaagccat gcacaagtgc atcttgaagc ccctcaaggg gcacgtggag 1200
gccatgctga aggactttca catggccgat ggctcatgga agcaactcaa ggagaacctg 1260
cagettgtge ggeagaggaa teegeaggag etgggggtet tegeceegae eeetgatttt 1320
gtggatgtgg agaaaatcaa agtcaagttc atgaccatgc agaagatgta ttcgccggaa 1380
aagaaggtca tgctgctgct gcgggtctgc aagctcattt acacggtcat ggagaacaac 1440
tcagggagga tgtatggcgc tgatgacttc ttgccagtcc tgacctatgt catagcccag 1500
tgtgacatgc ttgaattgga cactgaaatc gagtacatga tggagctcct agacccatcg 1560
ctgttacatg gagaaggagg ctattacttg acaagcgcat atggagcact ttctctgata 1620
aagaatttcc aagaagaaca agcagcgcga ctgctcagct cagaaaccag agacaccctg 1680
aggcagtggc acaaacggag aaccaccaac cggaccatcc cctctgtgga cgacttccag 1740
```

```
aattacctcc gagttgcatt tcaggaggtc aacagtggtt gcacaggaaa gaccctcctt 1800
gtgagacctt acatcaccac tgaggatgtg tgtcagatct gcgctgagaa gttcaaggtg 1860
ggggaccctg aggagtacag cctctttctc ttcgttgacg agacatggca gcagctggca 1920
gaggacactt accetcaaaa aatcaaggeg gagetgeaca geegaceaca geeceacate 1980
ttccactttg tctacaaacg catcaagaac gatccttatg gcatcatttt ccagaacggg 2040
gaagaagacc tcaccacctc ctagaagaca ggcgggactt cccagtggtg catccaaagg 2100
ggagctqqaa gccttgcctt cccqcttcta catgcttgag cttqaaaagc agtcacctcc 2160
teggggacce eteagtgtag tgactaagce atecacagge caacteggee aagggeaact 2220
ttagccacgc aaggtagctg aggtttgtga aacagtagga ttctcttttg gcaatggaga 2280
attgcatctg atggttcaag tgtcctgaga ttgtttgcta cctaccccca gtcaggttct 2340
aggttggctt acaggtatgt atatgtgcag aagaaacact taagatacaa gttcttttga 2400
attcaacage agatgcttge gatgcagtge gtcaggtgat teteacteet gtggatgget 2460
gccttcgggt tttaaa
<210> 70
<211> 1415
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1901373CB1
gcgaggacgc gggacgagcc ggaagtggag tgcgctgcgg cgcgagctgg gccggcgggc 60
gtggttcgag agcgcgcaga gtccagactg gcggcagggc ccgaggggcc gacccgcagc 120
gtccctggtc tctccagccc tcactcggaa ccgcactgac aataccctcc cctcccttgg 180
gctggacccc tctctacagc taggagccaa tggcagaaga caaaaccaaa ccgagtgagt 240
tggaccaagg gaagtatgat gctgatgaca acgtgaagat catctgcctg ggagacagcg 300
cagtgggcaa atccaaactc atggagagat ttctcatgga tggctttcag ccacagcagc 360
tgtccacgta cgccctgacc ctgtacaagc acacagccac ggtagatgga aggaccatcc 420
ttgtggactt ttgggacacg gcaggccagg agcggttcca gagcatgcat gcctcctact 480
accacaaggc ccacgcctgc atcatggtgt ttgatgtaca gaggaaagtc acctatagga 540
acctgageac ctggtataca gagetteggg agtteaggee agagateeca tgcategtgg 600
tggccaataa aattgatgca gacataaacg tgacccaaaa aagcttcaat tttgccaaga 660
agtteteect geceetgtat ttegtetegg etgetgatgg taccaatgtt gtgaagetet 720
tcaatgatgc aattcgatta gctgtgtctt acaaacagaa ctcccaggac ttcatggatg 780
agatttttca ggagctcgag aacttcagct tggagcagga agaggaggac gtgccagacc 840
aggaacagag cagcagcatc gagaccccat cagaggaggt ggcctctccc cacagctgag 900
gggctggggc taggggtggg tggagccctt ttaaaatacc cttcccttca acaactctcc 960
agctetgaat ggagaaacte tetaggeeat eccetettet accteetgea acceaeceat 1020
cctattagcc tcccacattc aaggcccgtg atacagggat gaggtcagca ccagcaaact 1080
ctggactggt ggaagaattc cccaccagat ctccttgaag cagaattagg gatcagcatc 1140
attaacacct tececacce eteceegcag geagacagtg aagagaatca gaaaacatga 1200
ttatgtgtca ctttaataca ggaaatttag gtgttttttg gtgtttttgt ttttgttttt 1260
gttttctttc caaagctcac ctcggggaca attccttggg cttctcctga ggtaatgatt 1320
tacccccca cccacagctg agtctgtgag gccccatcct ttccctacgt tttctcccat 1380
cttttttcct cttcagtctc ccagtcatct ggttt
                                                                1415
<210> 71
<211> 1902
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2367767CB1
<400> 71
gegaggtetg getaggetae gggecaegeg eegeegeege tgeegeegee aetgteetet 60
teggaggege gggeeegaeg gaaaceatgt ttgtggeteg eageategeg geggaeeaea 120
aggateteat ecaegatgte tetttegaet tecaegggeg geggatggea acctgeteea 180
```

```
gcgatcagag cgttaaggtC tgggataaaa gtgaaagtgg tgattggcat tgtactgcta 240
gctggaagac acatagtgga tctgtatggc gtgtgacatg ggcccatcct gaatttgggc 300
aggittinge theetgitet titgacegaa cagetgetgi atgggaagaa atagtaggag 360
aatcaaatga taaactgcga ggacagagcc actgggttaa aaggacaact ctggtggata 420
gcagaacatc tgttactgat gtgaagtttg ctcccaagca catgggtctt atgttagcaa 480
cctgttccgc agatggtata gtaagaatct atgaggcacc agatgttatg aatctcagcc 540
agtggtcttt gcagcatgag atctcatgta agctaagctg tagttgtatt tcttggaacc 600
cttcaagctc tcgtgctcat tcccccatga tcgccgtagg aagtgatgac agtagcccca 660
acgcaatggc caaggttcag atttttgaat ataatgaaaa caccaggaaa tatgcaaaag 720
ctgaaactct tatgacagtc actgatcctg ttcatgatat tgcattcgct ccaaatttgg 780
qaaqatettt ccatatteta gcaatagega ccaaagatgt gagaattttt acattaaage 840
ctgtgaggaa agaactgact tcctctggtg ggccaacaaa gtttgaaatc catatagtgg 900
ctcagttcga taatcataat tctcaggtct ggcgagtgag ttggaatata acaggaacgg 960
tgctagcatc ttcaggagat gatgggtgtg taagattgtg gaaagctaat tatatggaca 1020
attggaagtg tactggtatt ttgaaaggta atgggagccc agtcaatggg agttctcagc 1080
agggaacctc aaatccttcc ctaggttcaa atattccaag tcttcagaat tcattaaatg 1140
gatcttctgc tggcagaaag cacagctgag tacaagctaa ctggagtaac tttgctgttt 1200
tgctgcttgt tgcatgcaca caggaatgga aagcgagctc cttttcccct tccccagcgc 1260
cgtttgacct ctcccaagat acaccagcag cctgcttact actaaacgca atccaaaagg 1320
cctttaaaaa tacagtgtat attttttgta ctagtcagtt tattgacact atttgaaact 1380
tttgaaatat aaacggagag gctttctgtt gagacattgt caccaaaaca attttttgaa 1440
atgttcctga aactaatttg ggtttaaaga ttaaaagggt tgttaccatt cttatctgag 1500
tagttgggag gaggggaata ccactttagt tcatttggaa aatatagaca tatttcttt 1560
gctttcttaa aacagcttaa aatgatgaac ttttataatt ttaatttgaa gattgaataa 1620
atatttttta taaagattgt tttgagtgct gatttgttta ctttttgtag atttgcttta 1680
tocatgatat toagtacaac totgtoattt otttgtaata titaaaaaaat attagtaaag 1740
qaqtqaatta ataaaqtaqt aataqtaaaa tgaaaggaac ttgactgtac agtttgtagc 1800
caggitaagc attiggtatt gittcattta caattiggga ciaagatgga aacactitti 1860
ttataagttt ttaattcata gtcactaaag agataaatgt tt
<210> 72
<211> 1681
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3090433CB1
<400> 72
gggcagggct ttgctatggc taatgatccc ttggaaggct tccatgaagt aaaccttgct 60
teacetactt eteeggacet tettggtgtg tatgaateag gaacteaaga geagactace 120
tcaccaagtg tcatctaccg gccacacct tcagctttat cctctgtacc tatccaggca 180
aatgcattag atgtttctga acttcctaca caacccgtgt attcatcccc cagacgttta 240
aattgtgcgg aaatatctag tatcagcttt catgttacag acccagcccc ttgctctacc 300
tctggagtca cagctggatt aactaaatta actacaagaa aggacaacta taatgcagag 360
agagagtttt tacagggtgc tactataaca gaggcttgcg atggcagtga tgatattttt 420
gggttgagta ctgatagtct gtctcgttta cgaagcccat ctgttttgga agttagagaa 480
aagggctatg aacgattaaa agaagaactc gcaaaagctc agagggaact gaagttaaaa 540
gatgaagaat gtgagaggct ttcaaaagtg cgagatcaac ttggacagga attggaagaa 600
ctcacagcta gtctatttga ggaagctcat aaaatggtga gagaagcaaa tatcaagcag 660
gcaacagcag aaaaacagct aaaagaagca caaggaaaaa ttgatgtact tcaagctgaa 720
gtagctgcat tgaagacact tgtattgtcc agttctccaa catcacctac gcaggagcct 780
ttgccaggtg gaaagacacc ttttaaaaag gggcatacaa gaaataaaag cacaagcagt 840
qctatgagtg gcagtcatca ggacctcagt gtgatacagc caattgtaaa agactgcaaa 900
gaggctgact tatccttgta taatgaattc cgattgtgga aggatgagcc cacaatggac 960
aggacgtgtc ctttcttaga caaaatctac caggaagata tetttccatg tttaacattc 1020
tcaaaaagtg agttggcttc agctgttctg gaggctgtgg aaaacaatac tctaagcatt 1080
gaaccagtgg gattacaacc tatccggttt gtgaaagctt ctgcagttga atgcggagga 1140
ccaaaaaaat gtgctctcac tggccagagt aagtcctgta aacacagaat taaattaggg 1200
gactcaagca actattatta tatttctcct ttttgcagat acaggatcac ttctgtatgt 1260
aactttttta catacattcg atacattcag cagggactcg tgaaacagca ggatgttgat 1320
cagatgtttt gggaggttat gcagttgaga aaagagatgt cattggcaaa gctgggttat 1380
```

```
ttcaaagagg aactctgatg ctctgcgtgg gaccatgcct gaactccccg aataactgaa 1440
aaatggctga atatttttat ggttacttga tatttatttc caaggagtga gcctaagact 1500
tttttcccct tttgcaaatt gctctaagaa gtaccatgat ttcttttaaa ctgatctatg 1560
ctqtqtttqc ttattcttta gttgaacaca ctatgaagaa ttccaggtgt actagtgaat 1620
gtaatttata gttgccaaaa aaaaaacaaa cctgaaataa ataaatgtta gattgaaaaa 1680
<210> 73
<211> 1378
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3800591CB1
<400> 73
ggcagatect atetggegea tgcgaaeget tetgtgeega tteettgaag ageaggegea 60
gactcaaggc tgttgcttcc gcccttactc cccgccgctc gtccctgggc ggggcgaagg 120
ctgggctggg ggaagaggcg tggcggcgct gtgcgcgtgc acaaaagaga gctgaggggc 180
gggggcgctg cggcacagct ggtttgagca actgaactgg aaacaagatg caggacccca 240
acqcaqacac tqaatqqaat gacatcttac gcaaaaaaggg tatcttaccc cccaaggaaa 300
gtctgaaaga attggaagag gaggcagaag aggagcagcg catcctccag cagtcagtgg 360
tgaaaacata tgaagatatg actttggaag agctggagga tcatgaagac gagtttaatg 420
aggaggatga acgtgctatt gaaatgtaca gacggcggag actggctgag tggaaagcaa 480
ctaaactgaa gaataaattc ggagaagttt tggagatctc agggaaggat tatgttcaag 540
aagttaccaa agctggcgag ggcttgtggg tcatcttgca cctttacaaa caaggaattc 600
ccctctgtgc cctgataaat cagcacctca gtggacttgc caggaagttt cctgatgtca 660
aatttatcaa agccatttca acaacctgca tacccaatta tcctgatagg aatctgccca 720
cgatatttgt ttacctggaa ggagatatca aggctcagtt tattggtcct ctggtgtttg 780
gcggcatgaa cctgacaaga gatgagttgg aatggaaact gtctgaatct ggagcaatta 840
tgacagacct ggaggaaaac cctaagaagc cgattgaaga cgtgttgctg tcctcagtgc 900
ggcgctctgt cctcatgaag agggacagcg attccgaggg tgactgaggc tacagcttct 960
atcacatgcc gaactttctt gtgacaaatt gtctgyattt tttaaaaaaag gaaaaagcaa 1020
gaatgaatcc ttgtggtttt tagttttgta taaattatgt ttcaaatctt tacattttgg 1080
aaataatcat tgctggagat tctgttaaat attttggaac tcttttttt ttaaattata 1140
gtatttcctc taaaaaaaat taaaaccagc catttgtatg gcaaaaaaaa aaaagatact 1200
tcaatattac aattcaggtt tcctaatttt ctaaaaccta tgggaatttt ctaggatgga 1260
cgatcttagg aaggatcact tttggctgtt gtgagaaaca caaaataatt ttattacact 1320
ttaaaaatgt tttgtcataa tttagttaat attaaccttg tttaacttta tagaaaga
<210> 74
<211> 1444
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5308471CB1
gcacgcagtg ccggaggccg cagcgccgga acctcagagg cgggtcgcag cggcgcagag 60
gaggtcagct gcgggagcgt ttccggggac ggtgccgcca tgagattgac cccgcgcgcg 120
ctgtgcagcg ccgcccaggc cgcctggcgg gagaacttcc ccctgtgcgg tcgcgacgtg 180
gcgcgctggt tcccgggcca catggccaag gggctgaaga agatgcagag cagcctgaag 240
ctggtggact gtatcatcga ggtccacgat gcccggatcc cactttcagg ccgcaaccct 300
ctgtttcagg aaaccttgg gcttaagcct cacttgctgg tcctcaacaa gatggacttg 360
qcqgatctta cagagcagca gaaaattatg caacacttag aaggagaagg cctaaaaaat 420
qtcattttta ccaactgtgt aaaggatgaa aatgtcaagc agatcatccc gatggtcact 480
gaactgattg ggagaagcca ccgctaccac cgaaaagaga acctggagta ctgtatcatg 540
gtcattgggg tccccaacgt gggcaagtcc tccctcatca actccctccg gaggcagcac 600
ctcaggaaag ggaaagccac cagggtgggt ggcgagcctg ggatcaccag agctgtgatg 660
tccaaaattc aggtctctga gcggcccctg atgttcctgt tggacactcc tggcgtgctg 720
```

```
gctcctcgga ttgaaagtgt ggagacaggc ctgaagctgg ccctgtgtgg aacggtgctg 780
gaccacctgg tcggggagga gaccatggct gactacctgc tgtacaccct caacaaacac 840
cagcgctttg ggtacgtgca gcactacggc ctgggcagtg cctgtgacaa cgtagagcgc 900
gtgctgaaga gtgtggctgt gaagctgggg aagacgcaga aggtgaaggt gctcacgggc 960
acgggtaacg tgaacgttat tcagcctaac tatcctgcgg cagcccgtga cttcctgcag 1020
actiticegce gtgggetget gggtteegtg atgetggace tegaegteet geggggeeae 1080
cccccqqctg agactttgcc ctgaacttgt ccgggtaggg agggccggag gcatgtggcc 1140
teccagacet cetgacetgg gtggttgagg etcaagacag etcaeceggt ecagaagete 1200
catgctggtc actagggtgc tgtgctctct ggcgccccac agcctggcca gctccaggga 1260
cccaqttgc agggcccaag caggtgggag tggacaccag gcttcccagt ggacgtccct 1320
gagcagetee geatgettgg tteteeegga getteetget caggeetett gagaaatgga 1380
tgctgtctca gaaggagtta aagctataac ctgtaacctt taaaatctca aaaaaaaaa 1440
                                                                  1444
aaaa
<210> 75
<211> 2067
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5324322CB1
<400> 75
qqcactgtcc accagcactc agagctccat tatgtcccca gctggggttg cagggtaggg 60
qqqactqqqq tqtcccccaq cctcaqcaqa cgqaqgqcct caggqatqaq qctqccagga 120
tagcgccaga gaagcagctc agagcaaggg ctcctgagtg ggggcagggc tggggagaag 180
gtcatggggg ggctgcagta ggggtggtca ttgtgcaggc tgagttgaga gaagtgggtg 240
gccatgttct cctcagacag aaactgcttg cgcagaggct ccctggggag agatggcaga 300
gaggcaggct gggatactga cacaggaggc agcctgttgg ggaccagagg tgacagagat 360
cttgttggga gtccctcct gccccaaac tcactgctcc tcctccaggc gccgcttggt 420
getcatgggc acageteete ggagagggga getggegtee aggeeceaag teaceeceaa 480
qqcqqcccqc ggqaqqcqct ggqcccctcc ctgggggcct cgctgcaagg gctgctgcag 540
gatcattggg ttttggggtc ctgcgggtgg gatctgggcg acaggggagg agtctctgag 600
ggcgtggcca agagaggatg ggcgtggctt taggcgggca cagccgcgag gttctgcgcg 660
ggcgcggaag acgggcggcg cgtggcggaa ggcaggcttg ctcctcgggg tgggggaggg 720
tatccggctt aagggggctg cggtggacac cacttcttaa tgtcgggggt cttcgcggcg 780
ctcacctogg ctcctagggt togggacggt acgcaccage caccttogcg ccgaaggcgg 840
tagggcgcca cggagaggaa ccgctctagg cacgtaaggc ctcgtgaggt tgcgtcgcgc 900
geggageact etgggaettg tagttetgga gatggagega getgtgeege tegeggtgee 960
tetgggtcag acagaggtgt tecaggeett geageggete catatgacea tettetecea 1020
qaqcqtctca ccatqtqqqa aqtttctqqc qqctqqcaac aattacqqqc agattqccat 1080
cttcagcttg tcctctgctt tgagctcaga agccaaagag gaaagtaaga agccggtggt 1140
gactttccaa gcccatgatg ggcccgtcta tagcatggtt tccaccgatc gacatctgct 1200
tagtgctggg gatggggagg tgaaggcctg gctttgggcg gagatgctca agaagggctg 1260
taaggagctg tggcgtcgtc agcctccata caggaccagc ctggaagtgc ctgagatcaa 1320
cgctttgctg ctggtcccca aggagaattc cctcatcctg gctgggggag actgtcagtt 1380
gcacactatg gaccttgaaa ctgggacttt cacgagggtc ctccggggcc acacagacta 1440
catccactgc ctggcactgc gggaaaggag cccagaggtg ctgtcaggtg gcgaggatgg 1500
agctgttcga ctttgggacc tgcgcacagc caaggaggtc cagacgatcg aggtctataa 1560
gcacgaggag tgctcgaggc cccacaatgg gcgctggatt ggatgtttgg caactgattc 1620
cgactggatg gtctgtggag ggggcccagc cctcaccctc tggcacctcc gatcctccac 1680
acccaccacc atottcccca teegggegee acagaageae gteacettet accaggacet 1740
gattetgtea getggeeagg geegetgegt caaccagtgg cagetgageg gggagetgaa 1800
ggcccaggtg cctggctcct ccccagggct gctcagcctc agcctcaacc agcagcctgc 1860
cgcgcctgag tgcaaggtcc tgacagctgc aggcaacagc tgccgggtgg atgtcttcac 1920
caacctgggt taccgagect tetecetgte ettetgatet etgacgaeae ecceagecag 1980
ctcagggttt tagagtgttt ttcattttct ttttttttt ttttttacaa taaagtttca 2040
ggctttttta ccaaaaaaaa aaaaaaa
                                                                  2067
<210> 76
<211> 2085
<212> DNA
```

. 74/115

```
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 067184CB1
<400> 76
gtgttgcgcg actggccttg agggagagct ggggcctgct cccggagaga tacggctatg 60
tcgatcgaaa tcgaatcttc ggatgtgatc cgccttatta tgcagtactt gaaggagaac 120
agtttacatc gggcgttagc caccttgcag gaggagacta ctgtgtctct gaatactgtg 180
gacagcattg agagttttgt ggctgacatt aacagtggcc attgggatac tgtgttgcag 240
gctatacagt ctctgaaatt gccagacaaa acceteattg acctetatga acaggttgtt 300
ctqqaattqa tagagctccg tgaattgggt gctgccaggt cacttttgag acagactgat 360
cccatgatca tgttaaaaca aacacagcca gagcgatata ttcatctgga gaaccttttg 420
gccaggtctt actttgatcc tcgtgaggca tacccagatg gaagtagcaa agaaaagaga 480
agagcagcaa ttgcccaggc cttagctggc gaagtcagtg tggtgcctcc atctcgtctc 540
atggcattgc tgggacaggc actgaagtgg cagcagcatc agggattgct tcctcctggt 600
atgaccatag atttgtttcg aggcaaggca gctgtcaaag atgtggaaga agaaaagttt 660
cctacacaac tgagcaggca tattaagttt ggtcagaaat cacatgtgga gtgtgctcga 720
ttttctccag atggtcagta tttggtcact gggtctgttg atggattcat tgaagtatgg 780
aactttacta ctqqaaaaat cagaaaggat cttaagtacc aggcccaaga taactttatg 840
atgatggatg atgctgtcct ctgcatgtgt ttcagcagag atacagaaat gttagcaact 900
ggggcccaag atggaaaaat caaggtgtgg aagattcaga gtggacaatg tttaaggaga 960
tttgagaggg cacacagtaa gggtgtcacc tgtctaagct tttctaagga tagcagtcag 1020
atccttagtg cttcttttga ccagacaatt agaattcatg gtttaaaatc tgggaaaacc 1080
ctgaaggaat ttcgtggcca ttcctccttt gttaacgaag caacatttac acaagatgga 1140
cattacatta ttagtgcatc ctctgatggc actgtaaaga tctggaatat gaagaccaca 1200
gaatgttcaa atacctttaa atccctgggc agcaccgcag ggacagatat taccgtcaac 1260
agtgtgattc tacttcctaa aaaccctgag cactttgtgg tgtgcaacag atcaaacacg 1320
gtggtcatca tqaacatqca ggggcagatt gtcagaagct tcagttctgg taaaagagaa 1380
ggtggggact ttgtttgctg tgccctctct ccccgtggtg aatggatcta ctgtgtaggg 1440
gaggactttg tgctctactg tttcagtaca gtcactggca aactggagag aactttgaca 1500
qtqcacqaqa aqqatqtgat tggtattgca catcaccctc atcagaacct gattgctacc 1560
tacagtgaag atggactcct aaagctctgg aaaccataat tcaacttttc tttttaaatc 1620
agctcgaaag catgtactta aatgaagcat attcatgtaa tgtgcttttt ttttttttt 1680
gccagctttt ctaagcaaat agattgtctg aattagtcac agaataattt tgtgaaaatt 1740
catgtttaag tagcaactac cotttettt tttatatatt tttaaggtat tagtttatet 1800
tettetaaet ggtgeagtea ettaatgttt teattaatet tegaeetgga gagtgaaata 1860
ctgatatttc tagaaaaaaa ttctactcct ctgattattt gaaatgctga ggaaaatgtc 1920
cctcccatag taaaacttgt aaataaggaa ctatatcata ttcagtagct gtgttctgtt 1980
ccatcttttt ttttttttt gagatggagt tttgcttgtt gcccaggctg gagtgcagcg 2040
gcacgatett ggttcactge aaccteegee teccaggtte aageg
<210> 77
<211> 2061
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 722896CB1
<400> 77
cgagccgcgg gacccgggcc gtaccgggga ggggccgctc cgggccgcag cgcgagggca 60
gcgaggggcg gcggggacct ggcaccgggc ggggccggcg gcagcgacca tgatcgcttt 120
gttcaacaag ctgctggact ggttcaaggc cctattctgg aaggaggaga tggagctcac 180
gctggtcggg cttcagtact cgggcaagac caccttcgtc aacgtgatcg cgtcaggaca 240
qttcaacgag gacatgatcc ccaccgtggg tttcaacatg cgcaaaatca ccaaagggaa 300
tgtgactatc aagctctggg acattggggg acagccgcgt ttccgcagca tgtgggagcg 360
ctactgccga ggagtgagcg ccatcgtgta catggtggat gctgctgacc aggagaagat 420
tgaggcctct aagaacgagc tccacaacct actggacaaa cctcagctgc agggcatccc 480
ggtcttagtc ctgggtaaca agcgagacct tccgggagca ttggatgaga aggagctgat 540
tgagaaaatg aatctgtctg ccatccagga ccgagagatc tgctgctact ccatctcttg 600
```

```
caaagaaaag gacaacattg acatcaccct acagtggctt attcaacact cgaagtcacg 660
gagaagctga gactccagcc cttctccctc agaccaggga ccgtcatcat ctaaacctga 720
agecquete ceegeccace cetgtegtee ecctaagece acceetecte acceagtgtg 780
aggagggcc tetggggacc ccagagtcct gttetgctga ggtttgaact cctgttttta 840
ttgtaaaata aattgcccc cattctggtc ccctaacttc tcacccttcc ccgctgcctt 900
tqtcccatca cccaqccctg cctccctccc agcagccctg ggccacagcc cccgcccttg 960
getttteece ggeeggtet tgtacetece tttteaacac tetetgttat tgteetgtgt 1020
gtacagtata tatatgtata tatattttaa tttttaatt taagcaaaga ctaaaatcaa 1080
ccatttgatg ctgcaggggc ctttcaggat ctgggagggg gcagtctgga gagaaggagg 1140
gagacgcagg tggacttggg gcaagttcag atcagaagag gtgcaggctg gcacctgcgg 1200
caggtaccag cctgggcact ggtggccgcc tccctgtccc gtgtgtttcc accgcccaat 1260
ctggcttqtc ctggcagtgc ttgaatgcca caggctggca ggggcctctg ggggccctc 1320
ccctcqaccc ccaqcctggg tagagccacc aggtacgacg accaggtacc agaaaccacc 1380
aggcacacgg ggcagaaagc cagcgtccat gccccagcag ccccctcctg cctgttcctg 1440
gctcccagct cccgcccctc cccagggccc ccacctccac ggcccacttc attttctgtt 1500
ctcatttige agagttgcae aaggagagaa ctcagcatgg ggggttggtt ctttgggttc 1560
tgtttgttta tttgtttaat ttaatgattt gtaaagtgat gttcctcttc cttttttaca 1620
cttttcagct catatttaac ctctgtttgg aaaatgattc ttgtaactgt acatttttt 1680
gcttcctaat aacaatgaca acaaaaaaaa taaatgacca gttttgtgtt ggggggggtg 1740
tatggtgctg gttacttttc cgcagttggc atgggttgcc ctacaggccc acagggccac 1800
cagcacacce ceqeaeqetq qqcaccaaca qagccacgga gegegageac atgccegece 1860
ggggagcaca atggcgctgc acaaaacggc ctcccacacg tgcgtccagg ctcttgcgcc 1920
acctecttet cattetett teagactite atgtagtece agetttgage cageagetge 1980
cacttggggc tgcagcgctc tgttgaggga actgcccagg gctgggtaga ggcagcaagg 2040
ggacagggct gggtgctgtt t
<210> 78
<211> 981
<212> DNA
<213> Homo sapiens
<221> misc_feature
<223> Incyte ID No: 1571739CB1
qtagttccag aaaataggac tgaccaagaa gcagaaaagc aagatgaatg atgtgaagct 60
tgctgtcttg ggtggtgaag gaacaggcaa atctgccctt acagtgaggt ttcttactaa 120
gcgattcatt ggagaatatg cttctaattt tgaatctatc tataagaagc acttgtgttt 180
ggaaaggaaa caactaaatc tagaaatata tgacccttgt tctcaaacac agaaagcaaa 240
attetecete acaagtgage tteactggge agatgggttt gttattgtgt atgacateag 300
tgataggtet teatttgett ttgcaaaage getgatetae agaateeggg ageeacaaac 360
tagtcattgt aaaagagctg tggaatcagc agtgtttttg gttggcaaca aacgagatct 420
ttgtcatgtg cgagaggttg gctgggaaga agggcaaaag ctggcactgg aaaaccgatg 480
ccaattctgt gaactgtctg cagcagagca gtctctggag gtggaaatga tgtttatcag 540
aattatcaag gacatcctga taaacttcaa actcaaagaa aagagacgtc ccagtggatc 600
taaatcaatg gccaaattga tcaataatgt atttggaaag agaaggaaat ctgtttagta 660
qacaggtaat cctgggagat ttcctatatc agagagtttc aaacattcac atgataatta 720
aactaacctt tgtatgcaat ttttttttgg taaaaagaat tctcttggag atatgaaatg 780
attgagtatg aaccacaget gtgttttcaa atatgtagtt tgeetttttg gttgttgtae 840
cctgctcact ctccttcaca cagaaccttt catttattgt acaacatcac actcacccta 900
acctactggc ggacagcgat cccagtttgc cttgccaaat aaactctgtt tatgtgaatt 960
tattaaacga caaaaaaaaa a
<210> 79
<211> 1375
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1739479CB1
```

```
<400> 79
aattetgtge tteteeetet tgggeettea cacaettatg ettatgtaaa taattattaa 60
cacagaatag gcattcagta aatatttttt gaatgattga ctgagaaatc acacctctgt 180
ttcttttaaa cacatcctga tagctccata agtttcatca gggtcagtgg tttccattgt 240
cctgactgct ggccacagtg acctgttctg tgctttattt gacaagaccc ctgaatggtt 300
ggacagtgat teetgecaaa agtgtgatea geetttette tggaaettea ageaaatgtg 360
ggacagtaag aaaattggtc taagacagca ccactgccgc aagtgtggga aggccgtctg 420
tggcaagtgc agctccaagc gctcctccat ccccctgatg ggcttcgagt ttgaagtgag 480
ggtctgtgac agctgccacg aggccatcac agatgaagaa cgtgcaccca cagccacctt 540
ccatgacagt aaacataaca tigigcatgi gcatticgat gcaaccagag gaiggitact 600
gacttctgga actgacaagg ttattaagtt gtgggatatg accccagtcg tgtcttgatg 660
actotoccag gaatcagaaa gatagtattt actaaagaaa cggttgtttt aacccaaatc 720
attaccagag tggtaaagca gacatgtgag aagtaagaaa gaaactaaag accctgaatg 780
aatttgcaga ttacccatgt gcacagtggg gacctggcca gtgagcactc gcaaggggac 840
tettecaact tgttcataca atataaaaga agetattttt ttaacaaatg gtttatacag 900
tetggetgtg etgeattgtt ttgagtgtae egaaaaatet gtgtggggtg tttaattttt 960
atacttttca acaccccatt ttatttgttg ctttgtcaga gaaataaggg aggtatctac 1020
tcagagtatt ttggtcatta tactttctgt gtttacttca acatgtgtca cgtggccagc 1080
ggetttttet tetetteet etgeacetae etgeacette tetgeettte etggagggga 1140
totatttato ttatttattc ccagtottc tottcato tcctcctcag togagagatt 1200
tqqaaactca tcatqtqqat tcaccagcca gctqctggaa ttgcctgaag agcgatttgt 1260
ttgtaatgtc tgcctcattc acgttcttat gaagtagaaa agactgtgtt tctgcctcag 1320
ttgcctctgt ctttcccaca ttaaaaaaaa aaatgctgtg agaaaaaaaa aaaaa
<210> 80
<211> 2833
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1999147CB1
<400> 80
eggttgggae geacacacte tgegteatgg agggetgagg eegatgatga atteeggagt 60
geetgteagg ettgetgtgt eacteggeee geteggegeg eccetteeea geegeeette 120
cgtaccggct ctcgggctct tccggtctcc ggccgcccct tacctgcagg ctcttctccc 180
geogeggee ggegetetee gagtegeee tgeggaetgg tetegeacag tgeetgggea 240
ccgggcgcca gacagacact ggccatgacg agcggcgcaa ccaggtaccg gctgagctgc 300
tegeteeggg gecacgaget ggacgtaegg ggeetggtgt getgegeeta teegeeggga 360
gcctttgtgt ccgtgtcccg agaccgcacc acccgcctct gggccccaga cagtccaaac 420
aggagettta cagaaatgca etgtatgagt ggecatteca attitigtate tigtigtatge 480
atcataccct caagtgacat ctaccctcat ggcctaattg ccaccggtgg aaatgaccac 540
aatatatgca ttttctcact ggacagtcca atgccacttt atattctaaa aggccacaaa 600
aatactgttt gtagtctatc atctggaaaa tttgggacat tacttagtgg ttcatgggac 660
accactgcta aagtctggct gaatgacaag tgcatgatga ccttgcaggg tcatacagct 720
gcagtgtggg cggtaaagat cttacctgaa cagggcttaa tgttgactgg atcagcagac 780
aagactgtta aactgtggaa ggctggaaga tgtgagagga ctttttcagg gcatgaagac 840
tqtgtaaqag gtttggcaat tttgagtgaa acagaatttc tttcctgtgc aaatgatgct 900
agtattagaa ggtggcaaat cactggcgag tgtcttgaag tatattatgg acatacaaat 960
tatatttata gcatatccgt ttttccaaat tgtagagact ttgtgacaac agcagaggac 1020
agatetetga gaatetggaa acatggggaa tgtgeteaaa etateegaet teeageteag 1080
tetatatggt getgetgtgt getegacaat ggtgacattg tggttggtgc gagtgatggc 1140
attattagag tgtttacaga atcagaagat cgaacagcaa gtgctgaaga aatcaaggct 1200
tttgaaaaag aactgtctca cgcaaccatt gattctaaaa ctggcgattt aggggacatc 1260
aatgctgagc agcttcctgg gagggaacat cttaatgaac ctggtactag agaaggacag 1320
actcgtctaa tcagagatgg ggagaaagtc gaagcctatc agtggagtgt tagtgaaggg 1380
aggtqqataa aaattqqtqa tqttqttggc tcatctggtg ctaatcagca aacatctgga 1440
aaagttttat atgaagggaa agaatttgat tatgttttct caattgatgt caatgaaggt 1500
qqaccatcat ataaattgcc atataatacc agtgatgacc cttggttaac tgcatacaac 1560
ttcttacaga agaatgattt gaatcctatg tttctggatc aagtagctaa atttattatt 1620
qataacacaa aaggtcaaat gttgggactt gggaatccca gcttttcaga tccatttaca 1680
```

```
ggtggtggtc ggtatgttcc gggctcttcg ggatcttcta acacactacc cacagcagat 1740
ccttttacag gtgctggtcg ttatgtacca ggttctgcaa gtatgggaac taccatggcc 1800
ggagttgatc catttacagg gaatagtgcc taccgatcag ctgcatctaa aacaatgaat 1860
atttatttcc ctaaaaaaga ggctgtcaca tttgaccaag caaaccctac acaaatatta 1920
ggtaaactga aggaacttaa tggaactgca cctgaagaga agaagttaac tgaggatgac 1980
ttgatacttc ttgagaagat actgtctcta atatgtaata gttcttcaga aaaacccaca 2040
qtccaqcaac ttcagatttt gtggaaagct attaactgtc ctgaagatat tgtctttcct 2100
qcacttgaca ttetteggtt gteaattaaa caccecagtg tgaatgagaa ettetgeaat 2160
gaaaaggaag gggctcagtt cagcagtcat cttatcaatc ttctgaaccc taaaggaaag 2220
ccagcaaacc agctgcttgc tctcaggact ttttgcaatt gttttgttgg ccaggcagga 2280
caaaaactca tgatgtccca gagggaatca ctgatgtccc atgcaataga actgaaatca 2340
gggagcaata agaacattca cattgctctg gctacattgg ccctgaacta ttctgtttgt 2400
tttcataaag accataacat tgaagggaaa gcccaatgtt tgtcactaat tagcacaatc 2460
ttggaagtag tacaagacct agaagccact tttagacttc ttgtggctct tggaacactt 2520
atcagtgatg attcaaatgc tgtacaatta gccaagtctt taggtgttga ttctcaaata 2580
aaaaagtatt cctcagtatc agaaccagct aaagtaagtg aatgctgtag atttatccta 2640
aatttgctgt agcagtgggg aagagggacg gatattttta attgattagt gtttttttcc 2700
tcacatttga catgactgat aacagataat taaaaaaaaga gaatacggtg gattaagtaa 2760
aattttacat cttgtaaagt ggtggggagg ggaaacagaa ataaaatttt tgcactgctg 2820
aaaaaaaaa aaa
<210> 81
<211> 1752.
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2182085CB1
<400> 81
gcaggcagcc atcttgcctg gagcctgaga aagggaggag agacagaagg aaccggcgac 60
agtggtctca gggccgctcc ggggggcctc aagaaccgga ggcagccccg gaggctgccg 120
cgggggaca cgccagagga ggaggccggg gaatggccgc ggtgtggcag caagtcttag 180
cagtggaege gaggtacaac gegtaeegea caceaaegtt tecacagttt eggaegeagt 240
atatccgccg gcgcagcagc tgctgcggga gaatgccaag gctgggcacc ccccagcgct 300
gcgtcggcag tacctgaggc ttcgggggca gctgctgggc cagcgctacg ggcccctctc 360
cgagccaggc agtgctcgtg cctatagcaa cagcatcgtc cgcagtagcc gcactactct 420
tgaccgcatg gaggactttg aggatgatcc tcgggccctg ggggcccgtg ggcaccgtcg 480
ttctgtcagc agaggctcct accagctgca ggcgcagatg aaccgtgccg tctatgagga 540
caggeceet ggeagegtgg tgeceaegte ageageagag geaagteggg ceatggeegg 600
qqacacqtca ctgagcgaga actatgcctt tgcgggcatg tatcatgttt ttgaccagca 660
ctgctcactc gacggcagca tctccctgtg ccagctggtg cctgccccac ccacagtgct 780
tegegtgeta eggggeeaca ecegtggtgt eteegaette geetggteee teteeaatga 840
catcetegtg tecaceteae tggatgecae catgegeate tgggeetetg aggatggteg 900
ctgcatccga gagatccctg accccgatag cgctgaactg ctctgctgca ccttccagcc 960
tgtcaacaac aacctcactg tggtggggaa cgccaagcac aacgtgcatg tcatgaacat 1020
ctccacaggc aagaaagtga aggggggctc cagcaagctg acaggccgtg tccttgctct 1080
gtcctttgat gcccctggcc ggctgctctg ggcgggtgat gaccgtggca gtgtcttctc 1140
tttcctcttt gatatggcca cagggaagct gaccaaagcc aagcgtttgg tggtgcatga 1200
ggggageeet gtgaccagea teteageeeg gteetgggte ageegegagg eeegggatee 1260
ctcactgctc atcaatgctt gcctcaacaa gttgctgctc tacagggtgg tagacaacga 1320
ggggaccetg cagetgaaga gaagetteee categageag ageteacate etgtgegeag 1380
catcttctgt cccctcatgt ccttccgcca gggggcctgc gtggtgacgg gcagtgagga 1440
catgtgcgtg cacttctttg atgtggagcg ggcggccaag gctgctgtca acaagctgca 1500
gggccacagt gcacctgtgc ttgatgtcag cttcaactgc gacgagagcc tactggcctc 1560
caqtgacgcc agcggcatgg tcatcgtctg gaggcgggag cagaagtagg gtcctgtcgg 1620
ccctgctgct gtcctccatc ccacccctct tactccagcc tcgtgttgta aataaagttt 1680
cggtggtcat gctgagggcc ggctcccagc tctgccgggg acggacaggg cagagggcag 1740
                                                                 1752
cgggcagctg ca
```

<210> 82

```
<211> 1854
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2216640CB1
<400> 82
cccacgcgtc cgcgcaggat ggcggcagca gtggcggacg aggcggtggc gcgcgatgtg 60
cageggttgc tagtgcagtt ccaggatgag ggcgggcagc tgctgggttc cccgttcgac 120
gtgcccgtgg acatcaccc ggacaggctg cagctcgtgt gcaacgcgct actggcccag 180
gaggatecee tgecactgge tttetttgte cacgatgetg agategtete etcactgggg 240
aagacgttgg agtcccaggc agtggagaca gagaaggtcc tagacatcat ctaccagcca 300
caggetatet teagagteeg ggetgtgaet egetgeacea geteettgga gggteacagt 360
gaggcagtca tttctgtggc cttcagccct acgggaaagt acctggccag tggctctgga 420
gacaccaccg tgcgcttctg ggatctcagc acagagacac cacatttcac atgcaaggga 480
cacagacact gggtccttag tatatcctgg tctccagatg gcaagaagct ggcctcaggc 540
tgcaagaatg gccagattct cctctgggac ccaagcacag ggaagcaggt gggcaggacc 600
ctcgctggcc acagcaagtg gatcacaggc ctgagctggg agcccctcca tgcgaaccct 660
gagtgccgct atgtggccag cagctccaag gatggcagtg tgcggatctg ggacacaact 720
qcaqqccqct qtqaqcgcat cctcaccggg cacacccagt cggtcacctg tctccggtgg 780
ggaggggacg ggcttctcta ctctgcctcc caggaccgca ccatcaaagt ctggagagct 840
catgacggtg tgctgtgccg gactctgcaa ggccacggcc actgggtgaa caccatggcc 900
ctcagcactg actatgccct gcgcactggg gcctttgaac ctgctgaggc ctcagttaat 960
ccccaagacc tccaaggatc cttgcaggag ttgaaggaga gggctctgag ccgatacaac 1020
ctcgtgcggg gccagggtcc agagaggctg gtgtctggct ccgacgactt caccttattc 1080
ctgtggtccc cagcagagga caaaaagcct ctcactcgga tgacaggaca ccaagctctc 1140
atcaaccagg tgctcttctc tcctgactcc cgcatcgtgg ctagtgcctc ctttgacaag 1200
tccatcaagc tgtgggatgg caggacgggc aagtacctgg cttccctacg cggccacgtg 1260
gctgccgtgt accagattgc gtggtcagct gacagtcggc tcctggtcag cggcagcagt 1320
gacagcacac tgaaggtgtg ggatgtgaag gcccagaagc tggccatgga cctgcccggc 1380
cacqcqqatq aggtatatgc tgttgactgg agtccagatg gccagagagt ggcaagtggt 1440
qqqaaqqaca aatgcctccg gatatggagg agatgagacg gcccgaagtt ctctctgacc 1500
cccacctcga ctcggcctct gccagctgcc ttccctgcca gagaacaaag gctgagatgg 1560
cagtgcacac accetececa ecagtgggga cetgagaatg egtgtggeet getgteeteg 1620
atagaccgga atggggtttt cccacagatc cccgcctgtg gcacacccca gagccagaaa 1680
tcgaaggtca caggaagttg tcactgaact tggcccgtgt ctgctactct gtaccttgct 1740
ggtacagaca ggggtggtgg gcagccaggc tctatgagtg ggcccctagt gtcagctctg 1800
tacagggtca gatcccaggt tctatgacca aataagtaac ttaaaaaaaaa aaaa
<210> 83
<211> 862
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2417361CB1
ggcgtggctt caacagactt tcttttgcct gtctttgtcc cagagcctct tccctggccc 60
tgctgagacc actgctctaa gaagagacca ccagactgag agaggactcc cagctgccct 120
cagageggag geegagtget geacageeae agetgetetg aageeettee atgaateeee 180
ggaagaaggt ggacctgaaa ctcattatcg tcggagccat tggtgtggga aagacctccc 240
tccttcacca atatgtgcac aagacgtttt atgaggaata ccagaccaca ctgggggcca 300
gcatcctctc caagattatc atattgggtg acacaacttt gaagttacag atctgggaca 360
egggeggtea ggageggtte egeteeatgg tgteeacgtt etacaaggge teegatgget 420
qcatcctage ttttgatgte accgaectgg agtettttga agecetggat atetggeggg 480
gtgatgtcct ggccaagatt gtccccatgg agcagtccta ccccatggtg ttgttgggga 540
acaagatcga tctggcagac cggaaggtac cccaggaagt agctcaaggc tggtgtagag 600
agaaagatat teettaettt gaagteagtg eeaagaatga cateaatgtg gtgeaagegt 660
ttgagatgct ggccagtagg gctctgtcga ggtaccagag catcttagaa aatcacctca 720
```

```
cagaatccat caagctctcg ccagaccagt caaggagcag atgctgctga cctccagacg 780
cctqctctgg aagcccagaa acagagcctg ccccgagcct qgtcacccca ggcttgagaa 840
caggtgacca tccccctcca gc
                                                                 862
<210> 84
<211> 1406
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2454384CB1
<400> 84
ctagagectg gggtetegge aactteegge ggegggaget geagagegea aggeeegeee 60
actgegegtg egetteggee eggeteetee tgegeeeeeg geecetgega etgggaettg 120
gtacggccgg gcggttggcg tcctctgcgg ctcctgccag gggcgggctt ttcaaatctt 180
ccctttgaag gagtggcgac ggcccggaca gttcgcgttg gagatggagg ggccgagcct 240
gaggggtcct gcgctccgcc tggcggggct tcccaccag caggactgca acattcaaga 300
aaaaatagac ttagaaattc gaatgcgaga aggaatatgg aaactccttt ctctgagcac 360
tcagaaagat caagttttac atgcagttaa gaatctcatg gtgtgcaatg ctcgactaat 420
ggcctataca tcggagctac agaaattaga agaacagatt gcaaatcaga ctggaagatg 480
tgatgtgaaa tttgaaagta aagaacgaac agcatgtaaa ggaaagattg ccatatcaga 540
tattcgaata ccactaatgt ggaaagactc tgatcacttc agcaataaag aacgatcacg 600
acgctatgcc attittigtt tattcaaaat gggagctaat gtgtttgata ctgatgtggt 660
gaatgtggat aaaacaatca cagatatatg ttttgaaaat gtaaccatat tgtaagtatt 720
ttttaatctt cagagaataa aaataattta aaattcttct tttttaaaag aaagttctta 780
ttattggttc tttggattca ttttatgttt aaatgtttaa gtgatcttta aatgtttaat 840
atgattttaa aaattatttt gttcagaaga agtccatttc tctatctgca gttttctgat 900
gtgaaataaa aatggaaatc ttgtaattac tattagcagt aaatatttga cttattagat 960
atgacccatt tttaaattgt taataaatat agttcagtta ttaacaaagc tatgcataca 1020
acagaatatc ctgtaatgtt atttgatata gagagaattt aagcataaaa caggattttt 1080
atctcatgta ggatatttgg ttgcagaaat actaaaatag tatagcgact ttatttacaa 1140
gatagteetg aagtacatge tatataggaa gagcaetttg aaatttttggg gtgttetttt 1200
tettatggtg cacttette atgtacttea aagcaataaa aaaaaatggg tgateteagg 1260
gctgttttta ttgtccctgc tcttttacag gctcatttta ttgtggtcat aatacagaac 1320
aagaaggaac teettgggta gecatagaaa teatttttaa ettacatagt tttteetgee 1380
ctccttcaaa ggttctatgt gcctaa
<210> 85
<211> 1184
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2610262CB1
geggttttgg tgcctgaage agggagegeg gagtegttee egagagagge ggeeaggeta 60
tgctcgccgg tttccggcgt tccgctccgg ccagccagag tctctgtctc aacctgtgtc 120
cgtgctccag cagtctcctc agcccggccc cgcggcgcg ttggcggcgg cgccccaggc 180
gegeeecete eteegatgge ggeggagate cageecaage etetgaceeg caageegate 240
ctgctgcagc ggatggaggg gtcccaggag gtggtgaata tggccgtgat cgtgcccaaa 300
gaggagggcg tcatcagcgt ctccgaggac aggacagttc gtgtttggtt aaagagagac 360
agtggacagt attggccaag cgtataccat gcaatgcctt ctccatgttc atgcatgtct 420
tttaacccgg aaacaagaag actgtccata ggtctagaca atggtacaat ctcagagttt 480
atattgtcag aagattataa caagatgact cctgtgaaaa actatcaagc gcatcagagc 540
aagcaatttg cctggcactg ctctgagagt gggcagcgcc tgggaggtta tcggaccagt 660
gctgtggcct caggcctgca atttgatgtt gaaacccggc atgtgtttat cggtgaccac 720
traggreaag taaraateet caaactggag caagaaaact gracectggt caraacatte 780
agaggacaca caggtggggt gaccgctctc tgttgggacc cagtccagcg ggtgttgttc 840
```

```
tcaggcagtt cagatcactc tgtcatcatg tgggacatcg gtgggagaaa aggaacagcc 900
atcgagetee aaggacacaa egacagagte caggeeetet eetatgeaca geacacgega 960
caattgatct cctgtggcgg tgatggtggg attgtcgtct ggaacatgga cgtggagagg 1020
caggageete tgtggagetg ettegtggtt atgataagtg etgtgtgatg etcacettgg 1080
gaggtctgcg acatatattg aagtcatctc taacctgaag tactgacaga ctttctggaa 1140
gaaaaggctt gtaggaggaa acttcagaat tctattaaat ggtg
                                                                  1184
<210> 86
<211> 2965
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2700075CB1
<400> 86
ggcaccactg tgaaggtctg ggacgcagcc aagcagcagc ccctgacaga gctggcagcc 60
catggggacc tggtgcagag cgccgtctgg agccgagatg gagccctggt gggcacggcg 120
tgcaaggaca agcagctgcg gatctttgac cccagaacaa agccgcgggc ctctcagagc 180
acgcaggccc atgagaacag cagggatagc cggctggcat ggatgggcac ctgggagcac 240
cttgtgtcta ctggattcaa ccagatgcgt gagcgcgaag tgaagctgtg ggacacgcgg 300
ttetteteea gegeeetgge etceeteace ttggacacet egettgggtg tetegtgeet 360
ctgctggacc ctgactctgg gctcctggtc ctggcaggaa agggcgagag gcagctgtac 420
tgttacgagg tggtcccgca gcagccggcg ctgagcccag tgacccagtg tgtcctggag 480
agogtgctgc gtggggctgc ccttgtgccc cggcaggcgc tggccgtcat gagctgcgag 540
gtactccgcg tcctacagct gagcgacaca gccatcgtgc ccatcggcta ccatgtgccc 600
cgcaaggctg tggagttcca cgaggacctg ttcccggaca ctgccggctg tgtgcctgcc 660
accgacccc atagctggtg ggctggggac aaccagcagg tgcagaaggt cagcctcaac 720
cccgcctgcc ggccccaccc gagcttcact tectgtctgg tgccccctgc ggagcccctc 780
cctgacacag cccagcctgc ggtgatggag acacccgtgg gtgatgcaga cgcaagcgag 840
ggtttctctt ccctcccag ttcgctgacc tcgcctcca cgccctccag cctggggccc 900
tcactctcca gcaccagtgg catcgggacc agccccagtt tgaggtcgct gcagagcctg 960
ctgggcccca gttccaagit ccgccatgct cagggcactg tcctgcaccg agacagccac 1020
atcaccaacc tcaaggggct caacctcacc acacctggtg agagtgacgg cttctgtgcc 1080
aacaagctgc gtgtggccgt gccgctgctc agcagcgggg gacaggtggc tgtgcttgag 1140
ctacggaagc ctggccgcct gcccgacacg gcactgccca cgctgcagaa tggggcagct 1200
gtgactgatc tggcctggga cccctttgac ccccatcgcc tcgctgtggc tggtgaggac 1260
gccaggatcc gactgtggcg ggtacccgca gagggcctgg aagaggtgct caccacgcca 1320
gagactgtgc tcacaggcca cacggagaag atctgctccc tgcgcttcca cccactggca 1380
gccaatgtgc tggcctcgtc ctcctatgac ctcactgttc gcatctggga ccttcaggct 1440
ggagetgate ggetgaaget geagggeeae caagaceaga tetteageet ggeetggagt 1500
cctgatgggc agcagctggc cactgtctgc aaggatgggc gtgtgcgggt ctacaggccc 1560
cggagtggcc ctgagcccct gcaggaaggc ccagggccca agggaggacg cggagctcgc 1620
attgtctggg tatgtgatgg tcgctgtctg ctggtgtctg gctttgacag ccaaagtgag 1680
cgccagctgc tcctatatga agctgaggcc ctggccggcg gacccttggc agtgttgggc 1740
ctggacgtgg ctccctcaac cctgctgccc agctacgacc cagacactgg cctggtgctc 1800
ctgaccggca agggcgacac ccgtgtattc ctgtacgagc tgctccccga gtcccctttc 1860
ttcctggagt gcaacagctt cacgtcgcct gacccccaca agggcctcgt cctcctgcct 1920
aagacggagt gcgacgtgcg ggaagtggag ctgatgcggt gcctgcggct gcgtcagtcc 1980
tccctggagc ctgtggcctt ccggctgccc cgagtccgga aagagttctt ccaggatgac 2040
gtgttcccag acacggctgt gatctgggag cctgtgctca gtgccgaggc ctggctgcaa 2100
ggcgctaatg ggcagccctg gcttctcagc ctgcagcctc ctgacatgag cccagtgagc 2160
caageeeece gagaggeeee tgetegtegg geeecateet cagegcagta cetggaagaa 2220
aagtctgacc agcaaaagaa ggaggagctg ctgaatgcca tggtggcaaa actggggaac 2280
cgggaggacc cactececca ggacteettt gaaggegtgg acgaggacga gtgggactag 2340
cctgcgcccc cgtcacctcc acctcacctg tgctgccact tcctagtgca cacctcacgg 2400
ctcatcctca agctggaaga tacctctctg gccccggcac atgtcacccc tgcactcctg 2460
ccttcccgtg ggcacttcca catcctctgg gcctctggca gttcccaggg actgtttca 2520
cctctgctgt ctctggggtc agctgctgct catcagctgc ccgctagcat gtggccaggg 2580
gtgcagggtg gcggggggtc agcagcatgt ccctgggcag gccctgggca ccctgtctcc 2640
cctggtctca ctgctgacct gggctggtcc cagcctggat tggcctcatc caggatcttt 2700
ggtcacccca cgctgcccca tcttgcctgc tgttccagtt ctggtcaagg gccttggggg 2760
```

```
ctgqccccc accaggcctt ctagagcagc accagtctca gggccctggg accagctgcc 2820
ctacttccca ggtttgtagc caggagaagg gggcatcaca gagctgatgg tccaataagg 2880
ggggtgtgag ccccgcaggg actggcccgc acctgccttg gatgttttca gcaattaaac 2940
tttttaagc tggcaaaaaa aaaaa
<210> 87
<211> 2823
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2786701CB1
<400> 87
cggaggcagc ctagcetege geceegeeg ttgettetge ceteeggeet tecegeegee 60
gtcgccggga ccagccgctc ggggccgggc tgatacagcc gcttcaccgt gcccctgccc 120
gcgaccatgg cctcctccga ggtggcgcgg cacctgctct ttcagtctca catggcaacg 180
aaaacaactt gtatgtcttc acaaggatca gatgatgaac agataaaaaag agaaaacatt 240
cgttcgttga ctatgtctgg ccatgttggt tttgagagtt tgcctgatca gctggtgaac 300
agatccattc agcaaggttt ctgctttaat attctctgtg tgggggaaac tggaattgga 360
aaatcaacac tgattgacac attgtttaat actaattttg aagactatga atcctcacat 420
ttttgcccaa atgttaaact taaagctcag acatatgaac tccaggaaag taatgttcaa 480
ttgaaattga ccattgtgaa tacagtggga tttggtgacc aaataaataa agaagagagc 540
taccaaccaa tagttgacta catagatgct cagtttgagg cctatctcca agaagaactg 600
aagattaagc gttctctctt tacctaccat gattctcgca tccatgtgtg tctctacttc 660
atttcaccga caggccactc tctgaagaca cttgatctct taaccatgaa gaaccttgac 720
agcaaggtaa acattatacc agtgattgcc aaagcagata cggtttctaa aactgaatta 780
cagaagttta agatcaagct catgagtgaa ttggtcagca atggcgtcca gatataccag 840
ttcccaacgg atgatgacac tattgctaag gtcaacgctg caatgaatgg acagttgccg 900
tttgctgttg tgggaagtat ggatgaggta aaagtcggaa acaagatggt caaagctcgc 960
cagtaccett ggggtgttgt acaagtggaa aatgaaaacc actgtgactt tgtaaagctg 1020
cgggaaatgc tcatttgtac aaatatggag gacctgcgag agcagaccca taccaggcac 1080
tatgagettt acaggegetg caaactggag gaaatggget ttacagatgt gggeecagaa 1140
aacaagccag tcagtgttca agagacctat gaagccaaaa gacatgagtt ccatggtgaa 1200
cqtcagagga aggaagaaga aatgaaacag atgtttgtgc agcgagtaaa ggagaaagaa 1260
gccatattga aagaagctga gagagagcta caggccaaat ttgagcacct taagagactt 1320
caccaagaag agagaatgaa gcttgaagaa aagagaagac ttttggaaga agaaataatt 1380
gettteeta aaaagaaage taceteegag atattteaca gecagteett tetggeaaca 1440
ggcagcaacc tgaggaagga caaggaccgt aagaactcca attttttgta aaacagaagt 1500
tccagagcac agaaggtcat catcacaagc aaactttatt aaaaaaaaac tagaagtgtg 1560
ctttgatttt gctgttattt gttttatcac ttctatattt ggtgaacagc cacagttact 1620
gatatttatg gaaaagtact ttcaagtaca aggtcaatac ataagccaga gtgaatgata 1680
ctacaagttg agcatctcta attcaaaaat ctgaaatcca gaagcttcaa aatctgaatc 1740
tttttgagca ctgacttgac cccacaagtg gaaaattccc cacccgacac ctttgctttc 1800
tgatggttca gtttaaacag attttgtttc ttgcacaaaa tttttgtata aattactttc 1860
aggctatatg tataaggtgg atgtgaaaca tgaattatgt aattagagtc gggtcccgtt 1920
gtgtatatgc agatattcca aacctgaaat ccaaaacact tctggtccct agcattttgg 1980
ataagggata ctcagcttgt acctatatat tcatatatat tcactgttgt tagaaatgtt 2040
taagttgctg ttctgtgatg aatctaaatc ttttctcttg ctaccaagct attgtcactg 2100
cagtgcatta taccaaagag cgaagtcagt gccactgaaa atacagaacc cattaatatc 2160
gtggctatct gattacattt atattccaag atgaaccttt tttatatatg ctaaaaattt 2220
tggggaatat gttttgggat gtattatgga gctaaaactc taacctctta atagttttat 2280
agaacttaaa aattttttat acaattaccc aattggtgat atgatcttaa gcttttgtgt 2340
cagattattt aatatgatga cttcatgctt tattatgcct tattatggct gacgtattac 2400
tgtggtgaaa caaaatatct ttaaaagtta aaacatccag atatataagc tattttttcc 2460
taaggataaa gtacctttga gcatgagtgt atcacagctt tcattaggaa aacttttcat 2520
tacatacttg tttaaactct gtcttccagg gtaaaaataa taaggttgaa tcattttatt 2580
aaaaatactt tttaagaaaa taactatgaa catctgaata ttaaagatat aaaaatgcac 2640
ataattcata tttcaggtgg tatttgcatt cagtgcctta ctggtattct cagaacattt 2700
taatgatttc taacatttct taacagtcat agatatatac attttcattt tttgtacttg 2760
aatattctaa ataaaactga catttactct tgacaaataa aacatatatt tactaaaaaa 2820
                                                                  2823
```

```
<210> 88
<211> 1549
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<223> Incyte ID No: 3068538CB1
gcagacccgg cacgcaggtg ggggccggcg gggtccgtgg ccagagctgc agagagacaa 60
ggcggcggcg gctgctgtgc tgggtgcagt gaggaagagg ccctcggtgg tgcccatggc 120
tggccaggat cctgcgctga gcacgagtca cccgttctac gacgtggcca gacatggcat 180
tctgcaggtg gcaggggatg accgctttgg aagacgtgtt gtcacgttca gctgctgccg 240
gatgccaccc tcccacgagc tggaccacca gcggctgctg gagtatttga agtacacct 300
ggaccaatac gttgagaacg attataccat cgtctatttc cactacgggc tgaacagccg 360
gaacaageet teeetggget ggeteeagag egeatacaag gagttegata ggaagtacaa 420
gaagaacttg aaggeeetet aegtggtgea eeceaceage tteateaagg teetgtggaa 480
catcttgaag cccctcatca gtcacaagtt tgggaagaaa gtcatctatt tcaactacct 540
gagtgagete caegaacaee ttaaataega eeagetggte ateceteeeg aagttttgeg 600
gtacgatgag aagctecaga geetgeacga gggeeggaeg eegeeteeca ecaaqacace 660
teegeegegg eeceegetge eeacaegea gtttggegte agtetgeaat aceteaaaga 720
caaaaatcaa ggcgaactca tccccctgt gctgaggttc acagtgacgt acctgagaga 780
gaaaggcctg cgcaccgagg gcctgttccg gagatccgcc agcgtgcaga ccgtccgcga 840
gatccagagg ctctacaacc aagggaagcc cgtgaacttt gacgactacg gggacattca 900
catecotyce gtgatectga agacetteet gegagagetg ecceageege ttetgacett 960
ccaggectac gageagatte tegggateae etgtgtggag ageageetge gtgteaetgg 1020
ctgccgccag atcttacgga gcctcccaga gcacaactac gtcgtcctcc gctacctcat 1080
gggcttcctg catgcggtgt cccgggagag catcttcaac aaaatgaaca gctctaacct 1140
ggcctgtgtc ttcgggctga atttgatctg gccatcccag ggggtctcct ccctgagtgc 1200
ccttgtgccc ctgaacatgt tcactgaact gctgatcgag tactatgaaa agatcttcag 1260
caccceggag gcacctgggg agcacggcct ggcaccatgg gaacagggga gcagggcagc 1320
tecgagtece etgatggeag ceagaagaeg tetetagtgt tgcgaacaet etgtatattt 1440
cgagetacet eccacacetg tetgtgcace tgtatgtttt ataacettgg catetgtaaa 1500
aataaccagc cattagatga attcagaacc ttctaatgaa aaaaaaaaa
<210> 89
<211> 1722
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5159072CB1
gcaagaggga gccggcccga cgcggaccgc ttccctgcag tgccccgagt cccqqqcccq 60
egeogeegee geeeggetee getegeggee cetetgtetg eaggegtgee eeggeggegg 120
cggagagccg tcctcggccg aggaggctgg gaaacgcgag cgcaggcggc agagaggcct 180
caacgccgtc cctttcgcca ccgccttttc cttgcctcgc gccgctgtgc atttctctcc 240
ttttcctttg tttttttggc ccctcgcggg tgtgggcatt gttggttagc aaaagtgcag 300
cctcaagatg gctgatggca acgaggatct gcgggctgac gacttgcctg ggccagcctt 360
cgagagctat gagtccatgg agcttgcctg ccccgctgag cgcagcggcc acgtagccgt 420
cagcgacggg cgccacatgt tcgtctgggg cggctacaag agtaatcaag tcagaggatt 480
atatgacttt tatctgccta gagaagaact atggatctac aacatggaga ctggaagatg 540
gaaaaaaatc aacactgaag gtgatgttcc tccttctatg tcaggaagct gtgctgtgtg 600
tgtagacagg gtgctgtact tgtttggagg acaccattca agaggcaata ccaataagtt 660
ctacatgctg gattcaaggt ctacagacag agtgttacag tgggaaagaa ttgattgcca 720
aggaatteet eeateateaa aggacaaact tggtgtetgg gtatataaaa acaagttaat 780
attttttgga gggtatggat atttgcctga agataaagta ttgggaactt ttgaattcga 840
tgaaacatct ttttggaatt caagtcatcc aagaggatgg aatgatcatg tacatatttt 900
agatactgaa acatttacct ggagccagcc tataactact ggtaaagcac cttcacctcg 960
```

```
tgctgcccat gcctgtgcaa ctgtcggaaa tagaggcttc gtgtttggag gcagatatcg 1020
agatgctaga atgaatgatc ttcactatct taatctggat acatgggagt ggaatgaatt 1080
aattccacaa ggcatatgcc cagttggtcg atcttggcac tcactaacac cagtttcttc 1140
agatcatctt tttctctttg gaggatttac cactgataaa cagccactaa gtgatgcctg 1200
gacttactgc atcagtaaaa atgaatggat acaatttaat catccatata ccgaaaaacc 1260
aaggttatgg cacacagctt gtgccagcga tgaaggagaa gtaattgttt ttggtggatg 1320
tgccaacaac ttgcttgtcc atcacagagc tgcacacagt aatgaaatac taatatttc 1380
agttcaacca aaatctcttg tacggctaag cttagaagca gtcatttgct ttaaagaaat 1440
gttagccaac tcatggaact gccttccaaa acacttactt cacagtgtta atcagaggtt 1500
tggtagtaac aacacttctg gatcttaagg cttcataaat aatgcctatg atcaccttgc 1560
atggacagca atcctgtaaa catcacagag tggcatcatt tgtataatta tatgcattgt 1620
tgtagtttgc acctgttggt tttaatgtgc atgtgaatgg cctagagaac ctatttttgt 1680
gtctaaagtt tacaataaat gtatttaaca ccaaaaaaaa aa
<210> 90
<211> 1264
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<223> Incyte ID No: 5519057CB1
<400> 90
agegegeget ettgeggtgg egtaatetet eageetttet gtgteteett teeteegeet 60
cagtttggtg cgggtcgggg gaatggctga ggagatggag tcgtcgctcg aggcaagctt 120
ttcgtccagc ggggcagtgt caggggcctc agggtttttg cctcctgccc gctcccgcat 180
cttcaagata atcgtgatcg gcgactccaa tgtgggcaag acatgcctga cctaccgctt 240
ctgcgctggc cgcttccccg accgcaccga ggccacgata ggggtggatt tccgagaacg 300
agcggtggag attgatgggg agcgcatcaa gatccagcta tgggacacag caggacaaga 360
acgattcaga aagagcatgg ttcagcacta ctacagaaat gtacatgctg ttgtcttcgt 420
gtatgatatg accaacatgg ctagttttca tagcctacca tcttggatag aagaatgcaa 480
acaacatttg ctagccaatg atataccacg gattcttgtt ggaaataaat gtgacttgag 540
aagtgccata caggtaccca cagacttggc acaaaaattt gctgacacac acagtatgcc 600
tttgtttgaa acgtctgcta aaaaccccaa tgataatgac catgtggaag ctatatttat 660
gaccttggct cataagctta agtgccacaa accattaatg cttagtcagc cccctgataa 720
tggaattatc ctgaagcctg aaccaaagcc tgcaatgacg tgctggtgct aaataacagt 780
ctttattata ttatctaatt ttgactaaag aaatactttt gaagtatgac agtattaagt 840
cataagattt aatctcaact ataatgggtc atcttgacac tttgctgttt gtcattgtca 900
cgcttttgta ttttgtatct acttaagttt gtcactgtga caacacagga aaagttggtt 960
ttcaggtgag attgaaaatg aagcaaagat aggatgaatc tgaacatctc tccatctaga 1020
gcccaatgaa ggaagcttca aatgagaaca tgatggaatc agtaaccatt caatcttttg 1080
tcctaggatt ggaaaaaaat gttaaaggtt taggacacac ctaatagtat gtcctttgaa 1140
tgggaagttt tcttaatagg ataaaaactg gtatttcctt ctccccagag tacttttttg 1200
ttttttccat agagacgggg tcttgctatg ttgtccaggc tggccttgag ctcctgggct 1260
caag
                                                                  1264
<210> 91
<211> 2640
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 035379CB1
<400> 91
cggccgaggg ggcatcatga agcgggctgg cggcgctqcg tcccgggcgc gcqcqqqcgg 60
gaggtgcttc ccaaggaccg tagatgcctc tctagagcat gagctcaggc aagagtgccc 120
getacaaceg etteteeggg gggeeeagea atetteecac eccagaegte accaeaggga 180
ccagaatgga aacgaccttc ggacccgcct tttcagccgt caccaccatc acaaaagctg 240
acgggaccag cacctacaag cagcactgca ggacacctt ctcttccagc acccttgcct 300
actoccegeg ggacgaggag gacagcatge cocccatcag cactoccege egetecgact 360
```

```
cogccatcte tgtccgctcc ctgcactcag agtccagcat gtctctgcgc tccacattct 420
cactgcccga ggaggaggag gagccggagc cactggtgtt tgcggagcag ccctcggtga 480
agetgtgctg tcagetctgc tgcagegtct tcaaagaccc cgtgatcacc acgtgtgggc 540
acacgttctg taggagatgc gccttgaagt cagagaagtg tcccgtggac aacgtcaaac 600
tgaccgtggt ggtgaacaac atcgcggtgg ccgagcagat cggggagctc ttcatccact 660
qccqqcacgg ctgccgggta gcgggcagcg ggaagcccc catctttgag gtggacccc 720
qaqqqtgccc cttcaccatc aagctcagcg cccggaagga ccacgagggc agctgtgact 780
acaggeetgt geggtgteee aacaaceeca getgeeeece getgeteagg atgaacetgg 840
aggcccacct caaggagtgc gagcacatca aatgccccca ctccaagtac gggtgcacgt 900
tcatcgggaa ccaggacact tacgagaccc acctggagac ttgccgcttc gagggcctga 960
aggagtttct gcagcagacg gatgaccgct tccacgagat gcacgtggct ctggcccaga 1020
aggaccagga gatcgccttc ctgcgctcca tgctgggaaa gctctcggag aagatcgacc 1080
agctagagaa gagcctggag ctcaagtttg acgtcctgga cgaaaaccag agcaagctca 1140
gcgaggacct catggagttc cggcgggacg catccatgtt aaatgacgag ctgtcccaca 1200
tcaacgcgcg gctgaacatg ggcatcctag gctcctacga ccctcagcag atcttcaagt 1260
gcaaagggac ctttgtgggc caccagggcc ctgtgtggtg tctctgcgtc tactccatgg 1320
gtgacctgct cttcagtggc tcctctgaca agaccatcaa ggtgtgggac acatgtacca 1380
cctacaagtg tcagaagaca ctggagggcc atgatggcat cgtgctggct ctctgcatcc 1440
aggggtgcaa actctacagc ggctctgcag actgcaccat cattgtgtgg gacatccaga 1500
acctgcagaa ggtgaacacc atccgggccc atgacaaccc ggtgtgcacg ctggtctcct 1560
cacacaacgt gctcttcagc ggctccctga aggccatcaa ggtctgggac atcgtgggca 1620
ctgagctgaa gttgaagaag gagctcacag gcctcaacca ctgggtgcgg gccctggtgg 1680
ctgcccagag ctacctgtac agcggctcct accagacaat caagatctgg gacatccgaa 1740
cccttgactg catccacgtc ctgcagacgt ctggtggcag cgtctactcc attgctgtga 1800
caaatcacca cattgtctgt ggcacctacg agaacctcat ccacgtgtgg gacattgagt 1860
ccaaggagca ggtgcggacc ctcacgggcc acgtgggcac cgtgtatgcc ctggcggtca 1920
tctcgacgcc agaccagacc aaagtcttca gtgcatccta cgaccggtcc ctcagggtct 1980
ggagtatgga caacatgate tgcacgcaga ceetgetgeg teaccagage agtgteaceg 2040
cgctggctgt gtcccggggc cgactcttct caggggctgt ggatagcact gtgaaggttt 2100
ggacttgcta acaggatcca ggccaggctg tggtttcccc tgaaccagcc ctggaccttt 2160
ctgagccagg ctggccacat ggggtggtct cggggtttct gcctgccccg tgggcatagg 2220
tggacagget ctggcagccg ggcagtgccc tccccgtccc atgctcggcg agcctccctc 2280
tactoggoac tgtccttgct gcccagccc tctctgggtg ccaggtacga cgcttgccc 2340
ggcccacct ccatcccac cctccatccc caccctagat ggagcgaggg cctttttact 2400
caccttttct accgttttta gactgtatgt agattggtta cctcctggtt gaaataaatg 2460
ctccacagac tgtggctgtg agtggggaca gctcctcggg acaagggggc tgtgtgtggc 2520
cttgaggttg gtgtgcacag gcactggctg ctgtgagtgg gggggcatgg ggcagtttcc 2580
tttggtggac cccaggactt cggcccactc cggggcctcc cctccctgct aggaggtaac 2640
<210> 92
<211> 2071
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 275354CB1
gtgggcggaa ctcctagcgg acacctcgtg gagtccggcc ggaagagcaa ccgagatgaa 60
ggtgaagatg ctgagccgga atccggacaa ttatgtccgc gaaaccaagt tggacttaca 120
gagagttcca agaaactatg atcctgcttt acatcctttt gaggtcccac gagaatatgt 180
aagagettta aatgetacca aactggaacg agtatttgca aaaccattee ttgetteget 240
ggatggtcac cgtgatggag tcaattgctt ggcaaagcat ccagagaagc tggctactgt 300
cctttctggg gcgtgtgatg gagaggttag aatttggaat ctaactcagc ggaattgtat 360
ccgtacaata caagcacatg aaggctttgt acgaggaata tgtactcgct tttgtgggac 420
ttcttttttc actgttggtg atgacaaaac tgtgaagcag tggaaaatgg atgggccagg 480
ctatggagac gaggaagagc cattacatac aatattagga aagacagtgt atactgggat 540
tgatcatcac tggaaagaag ctgtttttgc cacatgtgga cagcaagtag acatttggga 600
tgaacaaaga actaatccta tatgttcaat gacctgggga tttgacagta taagtagtgt 660
taaatttaac ccaattgaga catttetett gggaagttgt gcatetgaca ggaatatagt 720
actgtacgat atgaggcaag ctactccttt gaaaaaggtt atcttagata tgagaacaaa 780
tacaatctgt tggaacccta tggaagcttt catttttaca gcagcaaatg aagattataa 840
```

```
cttatatact tttgatatgc gtgcactgga cactcctgta atggtccata tggatcatgt 900
atctgcagtg cttgatgtgg attactctcc cactgggaag gagtttgtgt ctgctagttt 960
cgataaatct attcgaatct ttcctgtaga caaaagtcga agcagggagg tatatcatac 1020
aaagagaatg caacatgtta totgtgtaaa atggacttot gacagcaagt atattatgtg 1080
tggatctgat gaaatgaaca ttcgcctgtg gaaagctaat gcttctgaaa aattgggtgt 1140
gcttacatca cgagaaaaag cagccaagga ttataaccag aaattgaagg agaaatttca 1200
gcattatect catataaaac gtatageteg teategacat etaceaaaat etatetatag 1260
ccagattcag gaacagcgca tcatgaaaga agctcgtcga cgaaaggaag tgaatcgtat 1320
taaacacagc aagcctggat ctgtgccact tgtgtcagag aagaagaaac acgtagtggc 1380
agttgtaaaa taattggtat tootaacaat ootgatgtat aattatttgt tacttttgat 1440
ttgagaactc tacaaataaa agtgctggga ctagattaat tgcaaacatt ttagttatat 1500
gtgtagaget ttattgttac teettttage taccetgaaa aatgateett aaaggtggee 1560
tagttggtaa gactgtttta tccttaatct gcattcttct ttcattgtag aatacagtat 1620
ttgcaactca ttttttcttg tttttattac agatatactt actttctctt tgatctatta 1680
ttgtagacac tatacattca aattgacatt taagaccaaa catctcttat gttatcttta 1740
atattacttt gaataatgat tgcaatgatg tttcttcctg tgattccaca taacatttag 1800
aataatgatg tcaatttttt acaactgaat ttatttctag tgctttactt atatttggct 1860
ttttgactct tttaaaacaa tcagcctgca tttatataac ttttataaat aataatataa 1920
tttgggtcaa gttaagatat taaaagttcc tttcagcatt gaaactttgg cctatttttg 1980
gtaaataatt ttcaatctca ctaaatccta aatagctctg tgtaacatag gtttttcttt 2040
ttttaatcat aaacttaata aactttgtgg a
<210> 93
<211> 2149
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 311658CB1
cattattttt aaaaatatta cccactcttq ataqtqtatc tqcactqaqa cacqtactqq 60
aagctatata ttgtttgaca tcccaatcta aaacaactca tctttcttac ttatgactag 120
agttcctcct cttcatttat attctttct tggtgaacat cagtgtctac caatttctaa 180
atgcaaagga gaaagataca attttaagcg aaatggtggt gatatgcaca acttgcagaa 240
ggttacataa aacttgggtt ttcagagatg atttttctc ttcttttag gatatgttca 300
aggaatgagt gatttacttt cccctctttt atatgtgatg gaaaatgaag tggatgcctt 360
ttggtgcttt gcctcttaca tggaccaaat gcatcagaat tttgaagaac aaatgcaagg 420
catgaagacc cagctaattc agctgagtac cttacttcga ttgttagaca gtggattttg 480
cagttactta gaatctcagg actctggata cctttatttt tgcttcaggt ggcttttaat 540
cagattcaaa agggaattta gttttctaga tattcttcga ttatgggagg taatgtggac 600
cgaactacca tgtacaaatt tccatcttct tctctgttgt gctattctgg aatcagaaaa 660
gcagcaaata atggaaaagc attatggctt caatgaaata cttaagcata tcaatgaatt 720
gtccatgaaa attgatgtgg aagatatact ctgcaaggca gaagcaattt ctctacagat 780
ggtaaaatgc aaggaattgc cacaagcagt ctgtgagatc cttgggcttc aaggcagtga 840
agttacaaca ccagattcag acgttggtga agacgaaaat gttgtcatga ctccttgtcc 900
tacatctgca tttcaaagta atgccttgcc tacactctct gccagtggag ccagaaatga 960
cageceaaca cagataceag tgteeteaga tgtetgeaga ttaacacetg catgateaet 1020
gttcttgctt ttttgggaag agacactttg ttgcaaccct ttttcaagta cttgaaagtt 1080
gaaaatttga aatcttggta ttgatcatgc tttaaggttt atgtaaagaa agtgtactga 1140
tgttcttaca ttaaagcttt acaaagattt aaactaatta tttttgtagt tacttctacc 1200
aaatagcctt tccttttcga taacattcct cagtattttt atagccaagt acattttatt 1260
ttcttgctga tgaactggaa ttggataaat attgcaagtg gatgagttgg aaattatgca 1320
ctttgaaaaa cattcacttt gtttaagctt attgggtttc agatttgatt aaattaaatg 1380
tggaggcttt ctatagcatt ctaagctgag aagtagattg ttacccagta atgaaataaa 1440
aaataaaaat aaaaggattt ttttctctat tgtttacgac agtactcagc ttaaatattt 1500
atgctggtca aatgtgattt aaattggaca ttttcatcaa tgcagtctaa tgtgtagata 1560
aatatttcaa ccataataag tggattggca gtatattttt tacattgaac ttttcttcac 1620
ttgtatataa agattatata taagtactta tttatgagta taagaaaggt taggcatatt 1680
ttcattaact gaataaacga cttgatttat ataacctggt ttatcaaaat ttaacatggc 1740
ttcagtatga gatcttttc aaaactattt tcttaaacat ttatttcatg agattatgtt 1800
caaccctgta cctggtgtaa ttttaaaatt aattgcttgt aacctcactt tactaataat 1860
```

```
gtttattatc tttcctaata atgcattaac tgattaatca qqtqtttaaa tttttataaa 1920
atactettge aaaaagttta tttgaaaaat ttetagatgg teteatgagt tteaaaataa 1980
taatttttgt gtatgaacaa agctgttgtt tttaccatgc agtattgcat gattttaagt 2040
tatgtggaat taacataact gattttgttt taattgtaag ttgttaactc ctgtatatat 2100
cattaaaata aatctgaagt tgaagtagtg tttttagtta aattatact
<210> 94
<211> 2332
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1251632CB1
<400> 94
gccaccccag aactgggcag cagcctcaag aagaagaagc ggctctccca gtcagatgag 60
gatgtcatta ggctaatagg acagcacttg aatggcttag ggctcaacca gactgttgat 120
ctcctcatgc aagagtcagg atgtcgttta gaacatcctt ctgctaccaa attccgaaat 180
catgtcatgg aaggagactg ggataaggca gaaaatgacc tgaatgaact aaagccttta 240
gtgcattete etcatgetat tgtgaggatg aagtttttgc tgetgcagea gaagtaceta 300
gaatacctgg aggatggcaa ggtcctggag gcacttcaag ttctacgctg tgaattgacg 360
ccgctgaaat acaatacaga gcgcattcat gttcttagtg ggtatctgat gtgtagccat 420
gcagaagacc tacgtgcaaa agcagaatgg gaaggcaaag ggacagcttc ccgatctaaa 480
ctattggata aacttcagac ctatttacca ccatcagtga tgcttccccc acggcgttta 540
cagactetee tgeggeagge ggtggaacta caaagggate ggtgcetata teacaatace 600
aaacttgata ataatctaga ttctgtgtct ctgcttatag accatgtttg tagtaggagg 660
cagttcccat gttatacgca gcagatactt acggagcatt gtaatgaagt gtggttctgt 720
aaatteteta atgatggcac taaactagca acaggatcaa aagatacaac agttatcata 780
tggcaagttg atccggatac acacctgcta aaactgctta aaacattaga aggacatgct 840
tatqqcqttt cttatattgc atggagtcca gatgacaact atcttgttgc ttgtggccca 900
gatgactgct ctgagctttg gctttggaat gtacaaacag gagaactaag gacaaaaatg 960
agccagtctc atgaagacag tttgacaagt gtggcttgga atccagatgg gaagcgcttt 1020
gtgactggag gtcagcgtgg gcagttctat cagtgtgact tagatggtaa tctccttgac 1080
tcctgggaag gggtaagagt gcaatgcctt tggtgcttga gtgatggaaa gactgttctg 1140
gcatcagata cacaccagcg aattcggggc tataacttcg aggaccttac agataggaac 1200
ataqtacaaq aaqatcatcc tattatgtct tttactattt caaaaaatgg ccgattagct 1260
ttgttaaatg tagcaactca gggagttcat ttatgggact tgcaagacag agttttagta 1320
agaaagtate aaggtgttac acaagggttt tatacaatte atteatgttt tggaggccat 1380
aatgaagact tcatcgctag tggcagtgaa gatcacaagg tttacatctg gcacaaacgt 1440
agtgaactgc caattgcgga gctgacaggg cacacacgta cagtaaactg tgtgagctgg 1500
aacccacaga ttccatccat gatggccagc gcctcagatg atggcactgt tagaatatgg 1560
ggaccagcac cttttataga ccaccagaat attgaagagg aatgcagtag catggatagt 1620
tgatggtgaa tttggagcag acgacttctg tttaacttaa aattagtcgt attttaatgg 1680
cttgggattt ggtgcaaaca aacatgattg atagctggac agacatgctc gtcatgaaaa 1740
aagaaccatt tctgaagccc gattggggcc aaacatttac accttgcttc atagtaacca 1800
gttgagatga agcacgtcgt tagaacgttg ttggacacca tgttgaatta ttcccccatc 1860
ggttgtgaag aactgtgcta cattcaggct tacccattga actcagtata tatattttt 1920
ttccttcctg tcttttgtct ggcaggatac cattcttgtt gctcttctgt gtaatgaagt 1980
ttaaatgctt gtttggaaaa ctttatttaa cagtttagaa ggcttgatag aaagagtgca 2040
ttagtctgaa gagtatacat tggataggaa agaatttcct tcttttgttt ctccaaatct 2100
ttccgcctta tttagcttga gatctttgca gcttggttca tggattctag ccttgcccgt 2160
tgcgcaqtat atactgatcc agatgataaa ccagtgaact atgtcaaaaag cactctcaat 2220
attacattty acaaaaaqtt ttytactttt cacatagctt gttgccccgt aaaagggtta 2280
2332
<210> 95
<211> 1751
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
```

<223> Incyte ID No: 1331955CB1

```
<400> 95
gcccgaatcg actccggaga caacgccggg cgacgccacc tgcgcaggtc ccggaggccg 60
ctggtgtctg tgtacagggc gtqctgtctg tggaaacgcg aggqcacact agcactttcc 120
tggaaggacc ccagacccac caagccactc agtccctgga cgagtttcca ctcaccccga 180
ctgcctctgt caccgggtcc ctccaccctt gtctcctgtg cggccagcgt cagagccatg 240
gcgacggagg agaagaagcc cgagaccgag gccgccagag cacagccaac cccttcgtca 300
tccgccactc agagcaagcc tacacctgtg aagccaaact atgctctaaa gttcaccctt 360
gctggccaca ccaaagcagt gtcctccgtg aaattcagcc cgaatggaga gtggctggca 420
agttcatctg ctgataaact tattaaaatt tggggcgcgt atgatgggaa atttgagaaa 480
accatatotg gtcacaagct gggaatatoc gatgtagcot ggtcgtcaga ttctaacctt 540
cttgtttctg cctcagatga caaaaccttg aagatatggg acgtgagctc gggcaagtgt 600
ctgaaaaccc tgaagggaca cagtaattat gtcttttgct gcaacttcaa tccccagtcc 660
aaccttattg tctcaggatc ctttgacgaa agcgtgagga tatgggatgt gaaaacaggg 720
aagtgcctca agactttgcc agctcactcg gatccagtct cggccgttca ttttaatcgt 780
gatggatect tgatagttte aagtagetat gatggtetet gtegeatetg ggacacegee 840
tcaggccagt gcctgaagac gctcatcgat gacgacaacc ccccgtgtc ttttgtgaag 900
ttctccccga acggcaaata catcctggcc gccacgctgg acaacactct gaagctctgg 960
gactacagca aggggaagtg cctgaagacg tacactggcc acaagaatga gaaatactgc 1020
atatttgcca atttctctgt tactggtggg aagtggattg tgtctggctc agaggataac 1080
cttgtttaca tctggaacct tcagacgaaa gagattgtac agaaactaca aggccacaca 1140
gatgtcgtga tctcaacagc ttgtcaccca acagaaaaca tcatcgcctc tgctgcgcta 1200
gaaaatgaca aaacaattaa actgtggaag agtgactgct aagtcccttt gctcctgccc 1260
gcgagagact gtcgggaagt tgacccggat tggcaagaaa cagggtgtct tggaggtggt 1320
cccccagatc tgcgcctggg ggtcaggaca gggcctgatt tgagcctcct ctctgaagat 1380
gatttggccg agcggaaggt gtggaccacc ggaaagttct taaaagttgc tggtgacatt 1440
tettgecaat tetaacaetg tetagggaag agtteetagt etattgtgtt caaacagagt 1500
caacaaaagt ttttaatttt ttattacaga agggtgaagt tcaatttaac atgcgttgtg 1560
ttttttcagt aaacgttctg tatctttttg atattccatg acccagtgca cgctgtggcc 1620
tgtcaccgcc accgtggccc cgccagctgg cctccccttt ggcccacgcc ggccgccccc 1680
attetetget gegtagatge cetggeecag ggeetgaete tecatteceg ceagtagggg 1740
                                                                  1751
taccgagete g
<210> 96
<211> 1285
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1412614CB1
<400> 96
cggagaaaaa gctgacctaa tgaaactgtg gcaacgtcag cgcttgaggc ttgaagaggg 60
agacaagcta aaagaggata tocagttgtt toatgatggc atttgcacct ccaaaaaaca 120
cagatggtcc caaaatgcag acaaagatga gcacctggac acccctaaac catcagctat 180
tgaatgaccg ggtatttgaa gaaagaagag ccctgcttgg caaatggttt gacaaatgga 240
cagactetea aagaaqaaga ateeteacag geetgttgga gegetgeteg etgteecage 300
aaaagttctg ctgtcgaaag cttcaagaga aaattccagc agaagccctg gactttacaa 360
ccaagettee aagggtgtta tetttataca tettttettt cetggaeeet eggageettt 420
gtcgttgtgc acaggtgtgc tggcattgga agaaccttgc tgagctggac cagctctgga 480
tgctgaaatg tttacggttt aactggtaca tcaatttctc tccaactccc tttgagcagg 540
ggatctggaa gaagcactat attcaaatgg tgaaagaact tcatattacc aagcctaaga 600
cacccccaaa ggatggattt gtaatcgctg acgttcaact agttacaagc aattctccag 660
aggaaaaaca gtccccttta tcagcttttc ggtcctcttc ctctttaaga aagaagaata 720
actcagggga gaaagcactt ccaccctggc gatcttctga taagcaccca acagatatca 780
ttcgttttaa ttacctagac aaccgtgacc ccatggagac tgtccagcaa ggaagaagaa 840
aaagaaacca aataacccca gacttcagcc gacagtcaca tgataagaaa aataaattgc 900
aggacagaac taggctaaga aaagcacaat caatgatgtc gaggagaaat cccttcccac 960
tatgtcccta agtgccagct ctcccctaaa agttccagct catctcgcct ggcctccccc 1020
tgagtcagtg ggactcccag ccactgccac cacagctgaa attctcatgc agcatcctca 1080
```

caggcaccct gggccccaag catgactcat ccaggttcca gagccaaagt ggactgaaca 1140

```
tgggaagact tttattatag aaatgacaag atgctttgca cagtggagag ctgaatttac 1200
ttggctccca ttagaaactc tttcagctta agtacttatt gtggtagtga gtcctacggt 1260
atttcagtaa aaaggaattc atggc
<210> 97
<211> 3260
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1750781CB1
<400> 97
ccggaagacc gtcccggatg gcctcgggga ctgccagtgt gtggaggtga gctccgggat 60
tgccggcatt cccgcttctg ctggttgctt catgctgcag gctgcggccg tcagccctcg 120
ctcgcattgg tggcgctgag gtgccggggc agcaagtgac atgtcgtcgg gcctccgcgc 180
cgctgacttc ccccgctgga agcgccacat ctcggagcaa ctgaggcgcc gggaccggct 240
gcagagacag gcgttcgagg agatcatcct gcagtataac aaattgctgg aaaagtcaga 300
tetteattea gtgttggeec agaaactaca ggetgaaaag catgaegtae caaacaggea 360
cgagataagt cccggacatg atggcacatg gaatgacaat cagctacaag aaatggccca 420
actgaggatt aagcaccaag aggaactgac tgaattacac aagaaacgtg gggagttagc 480
tcaactggtg attgacctga ataaccaaat gcagcggaag gacagggaga tgcagatgaa 540
tgaagcaaaa attgcagaat gtttgcagac tatctctgac ctggagacgg agtgcctaga 600
cctgcgcact aagctttgtg accttgaaag agccaaccag accctgaagg atgaatatga 660
tgccctgcag atcactttta ctgccttgga gggaaaactg aggaaaacta cggaagagaa 720
ccaggagetg gtcaccagat ggatggctga gaaagcccag gaagccaatc ggcttaatgc 780
agagaatgaa aaagactcca ggaggcggca agcccggctg cagaaagagc ttgcagaagc 840
agcaaaggaa cctctaccag tcgaacagga tgatgacatt gaggtcattg tggatgaaac 900
ctctgtctct tccttcccag tcccccagga caatgtggat actcatcctg gttctggtaa 1020
agaagtgagg gtaccagcta ctgccttgtg tgtcttcgat gcacatgatg gggaagtcaa 1080
cgctgtgcag ttcagtccag gttcccggtt actggccact ggaggcatgg accgcagggt 1140
taagctttgg gaagtatttg gagaaaaatg tgagttcaag ggttccctat ctggcagtaa 1200
tgcaggaatt acaagcattg aatttgatag tgctggatct tacctcttag cagcttcaaa 1260
tgattttgca agccgaatct ggactgtgga tgattatcga ttacggcaca cactcacggg 1320
acacagtggg aaagtgctgt ctgctaagtt cctgctggac aatgcgcgga ttgtctcagg 1380
aagtcacgac cggactctca aactctggga tctacgcagc aaagtctgca taaagacagt 1440
gtttgcagga tccagttgca atgatattgt ctgcacagag caatgtgtaa tgagtggaca 1500
ttttgacaag aaaattcgtt tctgggacat tcgatcagag agcatagttc gagagatgga 1560
gctgttggga aagattactg ccctggactt aaacccagaa aqqactgaqc tcctgaqctg 1620
ctcccgtgat gacttgctaa aagttattga tctccgaaca aatgctatca agcagacatt 1680
cagtgcacct gggttcaagt gcggctctga ctggaccaga gttgtcttca gccctgatgg 1740
cagttacgtg gcggcaggct ctgctgaggg ctctctgtat atctggagtg tgctcacagg 1800
gaaagtggaa aaggttcttt caaagcagca cagctcatcc atcaatgcgg tggcgtggtc 1860
gccctctggc tcgcacgttg tcagtgtgga caaaggatgc aaagctgtgc tgtgggcaca 1920
gtactgacgg ggctctcagg gctgggagga ccccagtgcc ctcctcagaa gaagcacatg 1980
ggctcctgca gccctgtcct ggcaggtgat gtgctgggta tagcatggac ctcccagaga 2040
ageteaaget atgtggeact gtagetttge egtgaatggg atttetgaag atttgaetga 2100
ggtetetett ggcetggaag aataacactg aaaaaacctg acgetgeggt cacttageag 2160
aggeteaggt tettgeettg ggaaacacta etagetetga cettecatae etcaettggg 2220
ggagcacagg gccccgctgg gcctcctcac caacggcagt gccaaaatca gcccccacat 2280
caaggtggtg ttetetgtge tttetetegt cettecaaag teggttetgg cetaacgcat 2340
gtcccaacac cttgggttca tttgcccggt gaactcactt taagcattgg attaacggaa 2400
actocogaac tacagaccoc tocotggtgg gttgcatgaa tgtgtctcat tactgctgaa 2460
atgtecteac atetetteca etgttettea gagetttetg getetette eccacaaaat 2520
tegacacatt taaaaatete egtgtggett taaaaaatgg ttttttgttt ttttgtttt 2580
ttgaggtggg agaggatgtg tgaaaatctt ttccagggaa atgggttcgc tgcagaggta 2640
aggatgtgtt cetgtatega tetgeagaea eccagaaggt gggtgeacae tgcatgettg 2700
ggggtgccaa gggattcgag acctccaaca tacttgtctg aaggtggtga ttctggccat 2760
ggeceetetg ceaageetgt gtgegatgee ettggtgett tagtgeaaga ageetagget 2820
cagaagcaca gcagcgccat ctttccgttt caggggttgt gatgaaggcc aaggaaaaac 2880
atttatettt actattttae etaegtataa agttttagtt eattgggtgt gegaaacace 2940
```

```
ctttttatca cttttaaatt tgcactttat ttttttttt ccatgcttgt tctctggaca 3000
tttggggatg tgagtgttag agctggtgag agaggagtca ggcggccttc ccaccgatgg 3060
tectggcete cacetgeest etetteestg cetgateace gettteeaat ttgeeettea 3120
gagaacttaa gtcaaggaga gttgaaattc acaggccagg gcacatcttt tatttatttc 3180
attatgttgg ccaacagaac ttgattgtaa ataataataa agaaatctgt tatatacttt 3240
tcaaaaaaaa aaaaaaaaaa
<210> 98
<211> 1276
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1821658CB1
geggeaeece caaggaagae cageetgeet etggteggtt cetggegete tgegtttegt 60
gaccttgtcc agtagaaggc tatttaattt tcacaactgc ttgaattttg acatacaaga 120
tgaaqcaaqa tqcctcaaqa aatqctqcct acactqtqqa ttqtqaaqat tatqtqcatq 180
tggtagaatt taatcccttt gagaatgggg attcaggaaa cctaattgca tatggtggca 240
ataattatgt ggtcattggc acgtgtacgt ttcaggaaga agaagcagac gttgaaggca 300
ttcagtataa aacacttcga acatttcacc atggagtcag ggttgatggc atagcttgga 360
gcccagagac tagacttgat tcattgcctc cagtaatcaa attttgtact tcagctgctg 420
atatgaaaat tagattattt acttcagatc ttcaggataa aaatgaatat aaggttttag 480
agggccatac cgatttcatt aatggtttgg tgtttgatcc caaagaaggc caagaaattg 540
caagtgtgag tgacgatcac acctgcagga tttggaactt ggaaggagtg caaacagctc 600
attttgttct tcattctcct ggcatgagtg tgtgctggca tcctgaggag acttttaagc 660
taatggttgc agagaagaat ggaacaatcc ggttttatga tcttttggcc caacaggcta 720
ttttatctct tgaatcagaa caagtgccat taatgtcagc acactggtgc ttaaaaaaaca 780
ccttcaaagt tggagccgtt gcaggaaatg attggttaat ttgggatatt actcggtcca 840
gttatcctca aaataagaga cctgttcaca tggatcgagc ctgcttattc aggtggtcca 900
caattagtga aaatctgttt gcaaccactg gttatcctgg caaaatggca agccagtttc 960
aaattcatca tttaggacac cctcagccca tcctcatggg ttctgtagcc gttggatctg 1020
gactgtcctg gcatcgaact ctccctctgt gtgtaattgg aggagaccac aagctgttgt 1080
tttgggtgac tgaagtataa agtgttttct gtaccttaga ttcacaaact ttgtattttt 1140
agtacatatt ttgaagaatt tctatagtac atattttgaa gaatttttat atcaaatata 1200
ccgtatactt tagaaaatgt ctcagttgct tttattaaat aaaatgttga tggtttgaaa 1260
aattaaaaaa aaaaaa
                                                                 1276
<210> 99
<211> 3608
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1872574CB1
<400> 99
gttttggttc tagccgctcg ccgtccttgc aggctctgcc gtcggaaagc cgctcattct 60
tetttttet getgeegete egggteeggg ceatttteeg ggeegggege actaaggtge 180
geggeeeegg ggeeeagtat atgaeeegee gteetgetat eettegette eeeegeeeea 240
tgtggctgcg gggccgcggc ggcgctgccc actatggccc ggaaagtagt tagcaggaag 300
cggaaagcgc ccgcctcgcc gggagctggg agcgacgctc agggcccgca gtttggctgg 360
gateactege tteacaaaag gaaaagaett ceteetgtga agagateett agtatactae 420
ttgaagaacc gggaagtcag gctacagaat gaaaccagct actctcgagt gttgcatggt 480
tatgcagcac agcaacttcc cagteteetg aaggagagag agttteacet tgggaccett 540
aataaagtgt ttgcatctca gtggttgaat cataggcaag tggtgtgtgg cacaaaatgc 600
aacacgctat ttgtcgtaga tgtccagaca agccagatca ccaagatccc cattctgaaa 660
gacegggage etggaggtgt gacecageag ggetgtggta tecatgeeat egagetgaat 720
cettetagaa cactgetage cactggagga gacaacccca acagtettge catetatega 780
```

```
ctacctacgc tggatcctgt gtgtgtagga gatgatggac acaaggactg gatcttttcc 840
ategeatgga teagegacae tatggeagtg tetggeteae gtgatggtte tatgggacte 900
tgggaggtga cagatgatgt tttgaccaaa agtgatgcga gacacaatgt gtcacgggtc 960
cctgtgtatg cacacatcac tcacaaggcc ttaaaggaca tccccaaaga agacacaaac 1020
cctgacaact gcaaggttcg ggctctggcc ttcaacaaca agaacaagga actgggagca 1080
gtgtctctgg atggctactt tcatctctgg aaggctgaaa atacactatc taagctcctc 1140
tccaccaaac tgccatattg ccgtgagaat gtgtgtctgg cttatggtag tgaatggtca 1200
gtttatgcag tgggctccca agctcatgtc tccttcttgg atccacggca gccatcatac 1260
aacgtcaagt ctgtctgttc cagggagcga ggcagtggaa tccggtcagt gagtttctac 1320
gagcacatca tcactgtggg aacagggcag ggctccctgc tgttctatga catccgagct 1380
cagagatttc tggaagagag gctctcagct tgttatgggt ccaagcccag actagcaggg 1440
gagaatctga aactaaccac tggcaaaggc tggctgaatc atgatgaaac ctggaggaat 1500
tacttttcag acattgactt cttccccaat gctgtttaca cccactgcta cgactcgtct 1560
ggaacgaaac tctttgtggc aggaggtccc ctcccttcag ggctccatgg aaactatgct 1620
gggctctgga gttaatgaca actccccaaa tgcagagatt tacactaact tccattctca 1680
gtttccttgt ttcttttgat ttttttttc ctaattgtgt gaggctcttg tgttttagtg 1740
ggaacaccaa agtttgccta tagtttaggc acttaatagg aagaagctct gtacagaaat 1800
ctgaaagttg ttttgctttt tgttttcccc tttggtaatc aaaattttac tatctttat 1860
tatttctggc ttttcaacca aacattgttg ctaatcccta tttttcttta agtgacacac 1920
attetectgt ctctggcttc ttcaggctga aatgacatag tctttctcac ccttacttca 1980
ctcttgagag gtagggctcc tttataatta catggttgct ctcagacttt ctgtgaaagt 2040
ttgggagctg tgtgtgtctg tgtgtgtgtg agagagagat cttgtctgcg tgtgtgtgtg 2100
tgatcttgtg tgcctgtagg tactgtgtgt cactgaaatt acctggagtg aggattactt 2160
gtaattaaaa tatttataaa agaaacaact ttattcacag agtccagctt tgggactagt 2220
ctgtatcttg ttttttaagt ctaacaacac tgataatagg aagtaaaaac agaaaggaaa 2280
agaaattacc actgggaaaa tctttttagt tagattgtag gcttcctggg gcctcccatg 2340
ccaggactgc aaagtgatcc agccctacct gtcttcccac ctgtgtgtcc cccgtgtggg 2400
aagttggtgt cactteeect teccaecete acatetgett agecagtage cacaececta 2460
aaacatcaga ctcaccatcc aggtgcagct ccagaggcta caaaaggctt catgggactt 2520
gaatccccat cctagettet eteteettee ecteaagace tgatetggtt ttaaggggee 2580
tggagetggg agteteaagt etgetaagat teacateeat ageeceegtg getttgagga 2640
gaatcctctc tgccattctt ccaatctccc cagtgggttt tgctattatt ttctaaattg 2700
ggttaagtct aagaaggtgg gggtgagcag ggggtttatc tgtgtgtagt gagtgcttca 2760
tgtgtggaat attcattttc ttactgcagt gggacttggg gttgaagcca cccctcctac 2820
tctgttggct tagccctgag atggtgacag gctggcctgc agtcagcatc attgtgcatg 2880
tgacagcatc aatgtgatta gtaatttgtc tgttcctccc ttgaactgtc tgtttagtct 2940
gaggttttta aacttgcagg cagctgactg tgatgtccac ttgttccctg atttttacac 3000
atcatgtcaa agataacagc tgttcccacc caccagttcc tctaagcaca tactctgctt 3060
ttctgtcaac atcccatttt ggggaaagga aaagtcatat ttattcctgc accccagttt 3120
tttaacttgt tctcccagtt gtcccctct tctctgggtg taagaaggga aattggaaaa 3180
aaaattatat atatattctc cttttaatgg tggggggcta ctggagagga gagacagcaa 3240
gtccacccta acttgttaca cagcacatac cacaggttct ggaattctca tcttcgaacc 3300
tagagaaata ggtgctataa acagggaatt aagcaaaatg ctggatgcta tagatctttt 3360
aattgtetta attitttte tattattaaa etacaggetg tagatttett agttetcaca 3420
gaacttctat cattttaaac tgacttgtat atttaaaaaa aaaatcttca gtaggatgtt 3480
ttgtactatt gctagaccct cttctgtaat gggtaatgcg tttgattgtt tgagattttc 3540
tgtttttaaa aatgtagcac ttgacttttt gccaaggaaa aaaataaaaa ttattccagt 3600
                                                                  3608
gcaaaaaa
<210> 100
<211> 1311
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2590967CB1
<400> 100
qqcaqgatga acgctgcttt ccaagatggc gacggaggga ggagggaagg agatgaacga 60
gattaagacc caattcacca cccgggaagg tctgtacaag ctgctgccgc actcggagta 120
cagceggece aacegggtge cetteaacte geagggatee aaceetgtee gegteteett 180
cgtaaacctc aacgaccagt ctggcaacgg cgaccgcctc tgcttcaatg tgggccggga 240
```

```
gctgtacttc tatatctaca agggggtccg caaggctgct gacttgagta aaccaataga 300
taaaaggata tacaaaggaa cacagcctac ttgtcatgac ttcaaccacc taacagccac 360
aqcaqaaaqt qtctctctcc tagtgggctt ttccgcaggc caagtccagc ttatagaccc 420
aatcaaaaaa gaaactagca aactttttaa tgaggaaggc tcattgtcat ccccaagcca 480
ggccaqttct ccaggtggaa ctgtagtgta gcgacctcac tgctgcgcgc acagtctccc 540
gggacttqga ctcgagggag tgacgaggag gagctccgag ctgcgcctga gccgtgccag 600
ccqqcqqacc tcaggcggtg gacgtcggcg atagccgtgt ggacggtgac cggctcactc 660
tgcggcgccg tgctcccgct gctcacccaa agaagttgtt tccattttaa accggtcttt 720
tggggctgca gtaaaaaata agaaatggag ttttcttgct ttttactcta aaattcaatg 780
taattaaatt tcatatatat ataatatata catatataca tagtgtaaaa taaaatgttt 840
cttggacaag aaatcccctg aaattcagct gttatagtgc ttcactgttt ttgcactgat 900
ttttctatac cttaggtggt cagaagacaa ccttgaatgc actcatagag aaaactgtta 960
ctttctgacg taatgtaatt caggaagaca gacgctgcaa tcacagattt taaaaaattg 1020
tttgcactta aaaatagttg aatgctggtg gaaagttact ttgcagatgg gtgtaaggac 1080
tcatggccct ctgaggtgcg gcgtgaagat gcccttttta cccgttgacg tttattttac 1140
gtaaaataaa ctgttgtttc caatgcaatc aactctgtat tatatgtata aatattgtaa 1200
ttctgcaatt ggggaaaata gttacttcac tagtaatttt catcatttaa gagtgatatt 1260
1311
<210> 101
<211> 2839
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2824491CB1
<400> 101
ggcctgcggg aagccaagat ggcgcatagg ggttctccag gctgcagttg gcgccttatc 60
agtatctaag cggagtgttt tggaaggagt taaggggctg tggcaaacgc cctctccgcc 120
gtcatggccc ggcatcggaa tgttcgaggc tataactacg atgaagattt tgaagatgat 180
gatetetaeg gecagtetgt agaggatgat tattgtattt egeegteaac agetgeteag 240
tttatttatt cacggcgtga caaaccttcc gttgagcctg tggaagaata tgattatgaa 300
gatctgaaag aatcttccaa ttctgtttca aaccatcagc tcagtggatt tgatcaagct 360
cytctttatt catgccttga tcacatgaga gaggtacttg gagatgctgt gccagatgaa 420
atattaattg aagcagttct gaagaacaag tttgatgtgc agaaggcttt gtcaggggtt 480
ctggaacaag atagagtgca gagtttgaag gacaagaatg aggcaacagt atctacagga 540
aagatagcaa aaggaaaacc agtagattcc cagacatcgc gaagtgaatc tgaaattgtg 600
ccaaaagttg ctaaaatgac tgtatctgga aagaagcaaa ctatgggatt tgaagtgcct 660
ggagtatctt ctgaagaaaa tggtcatagt ttccacacac ctcaaaaaagg accgcccatt 720
gaagatgcca ttgcttcttc cgatgttctt gagactgctt ctaaatctgc taatccaccc 780
cacacgattc aagcatcaga agagcagagt tcaaccccag caccggtgaa aaagtctggc 840
aagctgaggc agcaaataga tgtgaaggcg gaactggaga agcggcaagg agggaagcag 900
ctactcaact tagtggtcat tggtcatgtt gatgctggga aaagtactct gatgggccat 960
atgctttatc ttctgggtaa tataaacaaa agaactatgc ataagtatga acaggagtct 1020
aaaaaggctg gcaaagcttc gtttgcatat gcatgggtct tggatgaaac tggcgaagaa 1080
agggaaaggg gagtaaccat ggatgttggt atgacaaagt ttgaaaccac aaccaaagtt 1140
attacattaa tggatgctcc aggccataag gacttcattc caaatatgat tacaggagca 1200
gcccaggcgg atgtagctgt tttagttgta gatgccagca ggggagagtt tgaagctgga 1260
tttgagactg gaggacaaac acgagagcat ggactettgg teegttetet gggagtgacg 1320
cagcttgcag ttgcagttaa taaaatggat caggttaatt ggcaacaaga aaggtttcaa 1380
gagattactg gaaaacttgg gcactttctt aagcaagcag gttttaagga gagtgatgta 1440
ggttttattc ctacaagtgg tctcagtggt gaaaatctaa tcacaagatc tcagtcaagt 1500
gaactcacaa aatggtataa aggactatgt ttattagaac aaattgattc ctttaagcct 1560
ccccagcgat ctattgacaa accttttaga ttatgtgtgt ccgatgtttt caaagatcaa 1620
ggatctggat tttgcataac tggtaaaata gaagctggtt atatccaaac tggtgaccga 1680
ctactggcaa tgcctcctaa tgaaacttgt accgtgaaag gaatcactct gcatgatgaa 1740
cetgtegact gggeggeage aggegateat gttagtetta etttggttgg gatggatate 1800
atcaaaatca atgttggctg catattttgt ggccccaaaag tacccattaa agcttgcact 1860
cgtttcagag cccgaatcct catctttaat attgaaattc ctatcactaa aggatttcct 1920
gtgctgttac actaccaaac tgtcagtgaa cccgccgtta ttaaacgatt gattagtgtc 1980
ttaaacaaaa gcacgggtga agtcacaaag aaaaagccta agtttttgac taaaggccag 2040
```

```
aatqcattqq tagaqctaca gacacaaaga ccaatagctc ttgagctata taaagacttt 2100
aaagagetgg ggaggttcat gctacgttac ggtggttcta caatagetge tggtgttgte 2160
actgagataa aagaatgatg ggtcagaatt tctaccacgt ttctggatac agtgaaatag 2220
ctaacctctq tttcaagaat gcagttatta agtcaaagga acaatgtgca attgatatgt 2280
ttttagatga gagagaaaaa ttaaagctaa aattagctgc aaagaagtat taataatcac 2340
ctctgcaaaa attctaagtt gccaactggc aaagaaagtc taatgttaaa aacaactttg 2400
cctttgaaac gttaataaat ggatttactt tgctaagatt tatggcaagt gtcaaaaaata 2460
qtatctqaaq atactgaatc atcatgaaat gaactctact tctggccaaa gcacaatgta 2520
tttgcagttt tctcttttga ttcaattata ctgcacatgt tttaaggaaa agtaacttaa 2580
ttgggttttt caggcagttg atatttgacc taagcttttt ttttttttt tttttttt 2640
tccagttaat gctaagaaaa gatttgggga aggttataat aaaagtattt tgtggtgacc 2700
ataaqaatgt ccctcccaa acaagtaaac ttgtgaaagt ttaatttgga attagtggaa 2760
gctgttcctt tgaaagccaa gatattattt aagttgtaaa gccagctaat aaaatgcctt 2820
agtttgagca taaaaaaaa
<210> 102
<211> 1676
<212> DNA
<213> Homo sapiens
<221> misc_feature
<223> Incyte ID No: 2825460CB1
gggaggcgga ggttgaggtg agaggagatc gcgccattgc actccagcct gggcaacaag 60
ggcgaagttc tctcaaaaga aaaaaaaaaa tcgtcggttt ccttttccca tctttctttc 120
gtgacttata ttccagaacg aagccccaca catcattaat gatttgaatc gtttctaaag 180
tgtttcttaa atcgtttctt aaatcgtttg ttgtttcttg tctaacagtc cagaacacat 240
attacataat ggagccggga gacagactag ggctggcttg atccggccac gcagtccagg 300
aaaggtgctt ttcaccccca agtgcaaaat gatcaatgta ttcttccgat ctacataaac 360
aagcacctcc tggtttcatt ttcgtaaagc aaaacaagca tggaagcttt actgtttcgg 420
ctcttcaaac ttccaqcaac tacactqcqc tqcatcqqac tcqacqcccq ctggtgacqc 480
acacgctgcg ccggaagtgt gaactgtctg cctccaggct ttgtcatggc ggctgctgct 540
gcacgctgga accatgtgtg ggtcggcacc gagactggga tcttgaaagg ggtaaatctt 600
cagegaaaac aggeggegaa etteaeggee ggaggaeage egeggegega ggaggeagtg 660
agegeeetgt gttggggeae eggeggegag acceagatge tggtgggetg egeggaeagg 720
acqqtqaaqc acttcaqcac cgaggatggc atattccagg gtcagagaca ctgcccgggc 780
ggggagggca tgttccgtgg cctcgcccag gccgacggca ccctcatcac atgtgtggat 840
tctgggattc tcagagtctg gcatgacaag gacaaggaca catcctctga cccactcctg 900
gaactgagag tgggccctgg ggtgtgtagg atgcgccaag acccagcaca cccccatgtg 960
gttgccacag gtgggaaaga gaatgctttg aagatatggg acctgcaggg ctctgaggaa 1020
cctgtgttca gggccaagaa cgtgcggaat gactggctgg acttgcgggt tcccatctgg 1080
gaccaggaca tacagtttct cccaggatca cagaagcttg tcacctgcac agggtaccac 1140
caggicogtq titatgatec ageateceee cagegeegge cagteetaga gaccacetat 1200
ggagagtacc cactaacagc catgaccctc actccgggag gcaactcagt gattgtggga 1260
acceptcate ggcagctggc agaaattgac cttcggcaag ggcgtctact gggctgtctg 1320
aaggggctgg caggcagtgt gcgtgggttg cagtgccacc cttcaaagcc tctactagcc 1380
tectgtgget tggacagagt ettgaggata cacaggatee agaateeaeg gggtetggag 1440
cataaggatg agccccaaga gcctcaagaa cccaacaagg tgcccctaga agacacagag 1500
acagatgaac tttgggcatc cttggaggca gctgccaagc ggaagctctc gggtttggag 1560
cagececaag gageteteca aacgagaegg agaaagaaga ageggeetgg gtecaceage 1620
ccctgacgcc cctgtgccca ctttgtaaat aaactgctga acacccaaaa aaaaaa
<210> 103
<211> 3206
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2871116CB1
```

```
<400> 103
ccagagcgtg cgttcggtgg cccatagggg aagatggcgg ctgctccttt ggaggagcgg 60
gattgagagg atcggggtgg ggagaccaaa caagagagac atttctggct ctgaaggcga 120
acgetteget ggccatttag gagetetget caaagecaga egtateetag aaggaaaca 180
tcaccatggc tacagaaatt ggttctcctc ctcgtttttt ccatatgcca aggttccagc 240
accaggeace tegacagetg ttttataage gacetgattt tgcacaacag caagcaatge 300
aacagcttac ttttgatgga aaacgaatga gaaaagctgt gaaccgaaaa accatagact 360
acaatccatc tgtaattaag tatttggaga acagaatatg gcaaagagac cagagagata 420
tgcgggcaat tcagcctgat gcaggttatt acaatgatct ggtcccacct ataggaatgt 480
tgaataatcc tatgaatgca gtaacaacaa aatttgttcg gacatcaaca aataaagtaa 540
agtgtcctgt atttgttgtt aggctgcagg aagagtttga aagcctcagt gtccttaaat 600
cgtggactcc agaaggaaga cgcttggtca ctggagcttc tagtggggag tttaccctqt 660
ggaatggact cactttcaat tttgaaacaa tattacaggc tcacgacagc ccaqtgaqqq 720
ccatgacgtg gtcacataat gacatgtgga tgttgacagc agaccacgga ggatatgtga 780
aatattggca gtcgaacatg aacaacgtca agatgttcca ggcacataag gaggcgatta 840
gagaggccag gtttatacac aatataccat tttctgtagt ccctattgtc atggttaaat 900
tattctctaa gtgtattctg ggtgcagaga tgcatgggct ctgtcagttt ctgggaaact 960
ttctgcaccc tataaacaca atatttttct ttgttttcac acattcacca ttttgctggc 1020
acctttctga agtagtgttg tcccggtatc agcctttgca atatgttaga gatgtactgt 1080
ctgccgcatt ttgcactggt tttctctttt catttatgat taataatgtg tatacgttat 1140
teetttttat tatetaetgt gtaagacaag aatattteat teeaaataaa gaatteagte 1200
tttaattatg caactgaata aaatctaaag cctacagaaa acaacttcag aattcacaca 1260
aagtggaaaa aggcttaagt gaagacctgg ttggcttggt tatgccacga cttccaaagg 1320
aaagtatagg actaaaaccc tcacagataa ctggatgtgg caaacattaa cggagtaatg 1380
aatgggttct tcaagctttg cagctgtaag cagatcattg tcaagaagac tctaggactt 1440
ttettetgat teactgttga taacateact tatgeaaatg tatacaataa gtggagttta 1500
aaatattttc agtgagttgt atatttttac acatcagtga ggtatgtata gtaaaactgg 1560
gggaaaaagt tccaaataca agcctgaaga attgctgcag cctcagaata aagctaagca 1620
gcattettta aggttgtgcc acceatgtgt gggaggaggt tgacatettt atggaaacat 1680
catccactgt agtcatttgt tcatactttc agaatcttaa cagaaattgt tggatgaaca 1740
tgcttctgct ttgtagattt tgccttagtg tcatgcccat acattgagtt tacacagctg 1800
gtccttcata ggattccaaa gttcaaggga gtttttagag ttagttgaga aacttgatga 1860
tctttcactg ctgggaaaaa ctgactcctt cttgcagcag attctttggc tttacacaca 1920
agtetgaatg teettatttt aaagttttee teaaaggtge aacatteatg gaatagettg 1980
ccaggaagat gtgaaacttt tctacagacc tttgaaatgg atgagaaaca ttgtatgtag 2040
ggatgtttag caatcagtct tttaatagac agcccacatt gtttcagctt atttcatgaa 2100
gtgtctgagg cagaagctga tgataatttt gggagcagta ttcgtgtgtg atttaaaaga 2160
ctgcaggaat actgcaaaaa tagaatccat ttattttcac cacttaaggc agcttcatgt 2220
gatttcctcg tatcatagaa aatagagaag gaacatggat agcattagca ctaataatac 2280
acacttgaag ttctcagaat actgatgatt gaaaactcaa acaactgctc tgttgaagtc 2340
ttettttgat gagatgeeta tgttagetga egacatteae tttaaggget tetteaetgg 2400
attetteeet eteetgttta taatgeagea eagtgttttt attttteeet gtetgagaag 2460
cacagattat ctgttaaatg ctgacttctt tcccctgctg tgtgtcttca tgtaacagtt 2520
tctcacccac ggataataaa tttgctacat gctctgatga cggcactgtt agaatctggg 2580
actiticting tigccatgag gaaagaatto toogaggtac gigtactaac agtactgatt 2640
ggaatattta aatagggaag acatttgtgg ttaaatcatc acaaaaccac aatactggct 2700
tacacctcca ttcaattttt tttacatata cacaccgtct caggetette aaaaaaacce 2760
agcactttct ctgactcaca gtcattttgt aggtttttac taccagtgtt atctttgaat 2820
ttttcagctg taaattaaat acaagagtgc ctccccctta cttgcttatc tgtatgcatc 2880
ttttagggct gtattccttt tccttccttg tagccagggt acttgttccc aacatattga 2940
cactgtggtt tgatttagat agccgtcatt ctcctggcag tccttttaca atatgaatta 3000
accgacaaga tagaggtatc aaagctacac ttcttagtgt tactattttt gaaagcagtt 3060
ggtttttcag tacaccacat ttgtactaca tggccggctt gttactaagt tcgggtggca 3120
ttgctgcttg tttacttttg ttgattttat aattaataaa cctctatgaa attacttcat 3180
tccgtaactg aaaaaaaaa aaaaaa
<210> 104
<211> 921
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
```

```
<223> Incyte ID No: 2942212CB1
<400> 104
ggtgctgatg ctgctgccat ttcatcacct ttgcgagcgc acatccatcc ctccgctctc 60
coggegectg ggcctaccca gcttcgggct cccaggccag cgatgcgctc gcggctgagc 120
tagatectge egageegege tetetgagge gteggegggg egeeeetee egeegteece 180
qqtccqqqcc aaggagacct gcagagccgc ggccatggag gccatctggc tgtaccagtt 240
ccggctcatt gtcatcgggg attccacagt gggcaagtcc tgcctgatcc gccgcttcac 300
cgagggtcgc tttgcccagg tttctgaccc caccgtgggg gtggattttt tctcccgctt 360
ggtggagatc gagccaggaa aacgcatcaa gctccagatc tgggataccg cgggtcaaga 420
gaggttcaga tccatcactc gcgcctacta caggaactca gtaggtggtc ttctcttatt 480
tgccattacc aaccgcaggt ccttccagaa tgtccatgag tggttagaag agaccaaagt 540
acacqttcaq ccctaccaaa ttgtatttgt tctggtgggt cacaagtgtg acctggatac 600
acagaggcaa gtgactcgcc acgaggccga gaaactggct gctgcatacg gcatgaagta 660
cattgaaacg tcagcccgag atgccattaa tgtggagaaa gccttcacag acctgacaag 720
agacatatat gagctggtta aaagggggga gattacaatc caggagggct gggaaggggt 780
gaagagtgga tttgtaccaa atgtggttca ctcttcagaa gaggttgtca aatcagagag 840
gagatgtttg tgctagtcag ttcttttatt tccaaaacat gctctcctac ttgaactgaa 900
                                                                  921
aagtaagaga aataaataga a
<210> 105
<211> 1367
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3685151CB1
aagaggcacg tgcgctgctg aatggagctg gtcgctggtt gctacgagca ggtcctcttt 60
gggttcgctg tacacccgga gcccgaggct tgcggcgacc acgagcagca atggactctt 120
gtggctgact tcactcacca tgctcacact gcctccttgt cagcagtagc tgtaaatagt 180
cgttttgtgg tcactgggag caaagatgaa acaattcaca tttatgacat gaaaaagaag 240
attgagcatg gggctctagt gcatcacagt ggtacaataa cttgcctgac attctatggc 300
aacaggcatt taatcagtgg agcggaagat ggactcatct gtatctggga tgcaaagaaa 360
tgggaatece tgacgtcaat taaagctcac aaaggacagg tgacetteet ttetattcac 420
ccatctggca agttggccct gtcggttggt acagataaaa ctttaagaac gtggaatctt 480
gtagaaggaa gatcagcatt cataaaaaaat ataaaacaaa atgctcacat agtagaatgg 540
tccccaagag gagagcagta tgtagttatc atacagaata aaatagacat ctatcagctt 600
gacactgcat ccattagtgg caccatcaca aatgaaaaga gaatttcctc tgttaaattt 660
ctttcagagt ctgtccttgc agtggctgga gatgaagaag ttataaggtt ttttgactgt 720
gattcactag tgtgcctctg cgaatttaaa gctcatgaaa acagggtaaa ggacatgttc 780
agttttgaaa ttccagagca tcatgttatt gtttcagcat cgagtgatgg tttcatcaaa 840
atgtggaage ttaagcagga taagaaagtt cececatett taetetgtga aataaacaet 900
aatgccaggc tgacgtgtct tggagtgtgg ctagacaaag tggcagacat gaaagaaagc 960
cttcctccag ctgcagagcc ttctcctgta agtaaagaac agtccaaaat tggcaaaaag 1020
gagectggtg acacagtgea caaagaagaa aageggteaa aacetaacae aaagaaacge 1080
ggtttaacag gtgacagtaa gaaagcaaca aaagaaagtg gcctgatatc aaccaagaag 1140
aggaaaatgg tagaaatgtt ggaaaagaag aggaaaaaga agaaaataaa aacaatgcag 1200
tgaatcacag atgtctcctg aaagaactct tttagatgaa atcattctac tcaaatgtac 1260
cttaattttt ttttttccc tgagtaaaag caagaaattt cttcctttgg aaaaaatata 1320
tatattaaaa aaccactttt agatggtttt ttttaaaaaa aaaaaaa
<210> 106
<211> 1560
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
```

<223> Incyte ID No: 4881515CB1

```
<400> 106
aggeggactg gggaggeggc ggcctggctc ggcctggcct ggcctgtcag ggcgcgggcg 60
geggeggete cageaceatg teeetgeagt acggggegga ggagaegeee etegeeggea 120
gttacggcgc ggccgattcg tttccaaagg acttcggcta cggcgtggag gaggaggaag 180
aggaggegge ggeggegge ggaggggttg gggeagggge aggeggtgge tgtggteegg 240
ggggcgctga cagctccaag ccgaggattc tgctcatggg actccggcgc agcggcaagt 300
cctccatcca gaaggtggtg tttcataaga tgtcacccaa cgagaccctc tttttggaaa 360
gtaccaacaa gatttataag gatgacattt ccaatagctc ctttgtgaat ttccagatat 420
gggattttcc tgggcaaatg gacttttttg acccaacctt tgactatgag atgatcttca 480
ggggaacagg agcattgata tacgtcattg acgcacagga tgactacatg gaggctttaa 540
caagacttca cattactgtt tctaaagcct acaaagttaa cccagacatg aattttgagg 600
tttttattca caaagttgat ggtctgtctg atgatcacaa aatagaaaca cagagggaca 660
ttcatcaaag ggccaatgat gaccttgcag atgctgggct agaaaaactc catcttagct 720
tttatctgac tagtatctat gaccattcaa tatttgaagc ctttagtaag gtggtgcaga 780
aactcattcc acaactgccg accttggaaa acctattaaa tatctttata tcaaattcag 840
gtattgaaaa agcttttctc tttgatgttg tcagcaaaat ctacattgca acagacagtt 900
cccctgtgga tatgcaatct tatgaacttt gctgtgacat gatcgatgtt gtaattgatg 960
tgtcttgtat atatgggtta aaggaagatg gaagtggaag tgcttatgac aaagaatcta 1020
tggcaattat caagctgaat aatacaactg tcctttattt aaaggaggtg actaaatttt 1080
tggcactggt ctgcattcta agggaagaaa gctttgaaag aaaaggttta atagactaca 1140
acttecactg tttccgaaaa gctattcatg aggtttttga ggtgggtgtg acttctcaca 1200
ggagctgtgg tcaccagact agtgcctcca gtctgaaagc gctgacacac aatggcacgc 1260
cacgaaacgc catctagtct gaatcccagc gtcggggctc tgtgccagct tactcttcac 1320
tccagggtcg gatgccacgt gctacaggac atgggagctg ctgcttgtgg gaatctggtg 1380
cctgttccac tagagacaag gggtagagtt tctcatttgg atgaaaaccc cttcaactgg 1440
tggtgtacaa ctgaagctac tatatctttt ttgaaaatgg caaaaaaaaa aaaaaaaaat 1500
tctggagacc acagaactca agtgtgtgtt tctcctcttt tgggtcccct ttaagtagtt 1560
<210> 107
<211> 1495
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5324681CB1
gaagaggctc tgggctggca catgtgtatg gcggtgaggc gggcgggtac atggcgggct 60
ctgtgggact ggcgttgtgc gggcagacgt tggtggtgcg gggcggcagc cgattcctgg 120
ccacctccat agcaagcagt gatgatgaca gcctcttcat ctatgactgc agtgctgcag 180
aaaagaagtc acaagaaaat aaaggggagg acgcccctt ggaccagggg agcggtgcga 240
ttctggcgtc caccttctcc aagtctggca gctattttgc tttaaccgat gacagtaagc 300
qtctgattct tttccgtaca aaaccatggc aatgtctgag tgtcaggacc gtggcaagga 360
ggtgtacagc cctgactttc atagcctcgg aggagaaggt cttggtggcc gacaagtctg 420
gagacgtcta ctccttttcg gtgctggagc cacacgggtg tggccgtcta gagctggggc 480
acctgtctat gctgttagat gtggctgtga gtcctgatga ccgcttcatc ctcactgccg 540
accgggacga gaagatccga gtcagctggg ccgcggcgcc ccatagcatc gagtccttct 600
gettggggca cacagagttt gtgageegta teteegtggt gecaacteag eeegggetge 660
ttctgtcctc ctctggggac ggcaccctga ggctctggga gtacaggagc ggccgccagc 720
tgcactgctg tcacctggcc agtctgcagg agctggtgga cccccaggcc ccccagaagt 780
ttgccgcgtc caggattgca ttctggtgcc aggagaactg cgtggcgctc ctgtgcgacg 840
gcactcctgt ggtctacatc ttccagctgg acgcccgcag acagcagttg gtgtacaggc 900
agcagetgge gttecageae caagtgtggg acgtggettt cgaggagace caggggetgt 960
qqqtqctcca ggactqccag gaagcccccc tggtgctcta caggcctgtg ggcgaccagt 1020
ggcagtctgt tcctgagagc accgtgttaa agaaagtctc tggtgttctt cgtgggaact 1080
gggccatgct ggaaggctct gecggegeag acgccagctt cagcagtctc tacaaggcca 1140
cgttcgacaa cgtgacctcc tacctgaaga agaaagagga gagactgcag cagcagctag 1200
agaagaagca gcggcgcgg agtcccccgc ctgggcccga cgggcatgcc aagaagatga 1260
gaccggggga ggcgacgcta agttgctgat cgtggcggtc tgtttctgtc gactgtggac 1320
cacttatgtg cgatccgtgg accacttgcg tgcgatctgt cggccgacga tgagcttgtt 1380
cggatgtagc tccatcgtaa gtcgaggagc atctgtgatt tgtcctctgc ttatgggata 1440
tgtttttccg ctactgagtc tgtgtagtaa atttttgact aggaaaaaaa aaaaa
```

```
<210> 108
<211> 1919
<212> DNA
<213> Homo sapiens
<221> misc_feature
<223> Incyte ID No: 5387651CB1
cgccctgcat gcgagttggg ccgcgggcgg ggttggagcc tactcggggc gactgcgatg 60
gacgccttag aaggagagag ctttgcgctg tctttctcct ccgcctctga tgcagaattt 120
gatgctgtgg ttggatattt agaggacatt atcatggatg acgagttcca gttattacag 180
agaaatttca tggacaagta ctacctggag tttgaagaca cagaagagaa taaactcatc 240
tacacaccta tttttaatga atacatttct ttggtagaaa aatacattga agaacagctg 300
ctgcagcgga ttcctgagtt caacatggca gccttcacca caacattaca gcaccataag 360
gatgaagtgg ctggtgacat attcgacatg ctgctcacct tcacagattt tctggctttt 420
aaagaaatgt ttttggacta cagagcagaa aaagaaggcc gaggactgga cttaagcagt 480
ggcttagtgg tgacttcatt gtgcaaatca tcttctctgc cagcttccca gaacaatctg 540
cggcactagg tcctacctcc agccaatgaa tgggatcatt ctggatgtca ccagcccaat 600
aggeteaget catgatgaca gaacacatet tggaaagact gaetetgtta tgtaactett 660
catttatgtt aagtattaat aggtcaaaac caaaatgacc taaccctcct ggacctattt 720
atcctgaaac accttcttgt attcattaac catagtactc ctccccacct caagtagaca 780
cctctctcag gagettctga gtcagacgcc tctggagega gccctatgtc aggcactcca 840
cctggggggc ccttccccag catacctgct ggtgtgtaag tgtggactaa cccgccgcca 900
ccaccetetg ttccagcagg ctctgcatga atctttgtgc acttgcacct ctttttcaca 960
tgggccacag tttcagtact tcagcctcag tggggttcct gatgtttatc tagggtgtta 1020
ctcaagccca gtttgagatt ttggagtctc ctgtgatcac atcttgtctc ggctgtagga 1080
atcaacagaa ggagacgtcc tctacataaa agctccatgt gaaaagctac tcctagtctt 1140
aacatttgca gtccttgtgt cactgtcttc tggtcctgat gtagtcccac tgtttctaga 1200
agtetetttt aageattatt tttgaaaaaa aaaatatttt tatagatgaa taeteagget 1260
aacctagtgg atgtgatctt ggaacttcca tgattatcca cttaaagatc aaagtattat 1320
atgctgtgtg ctttttaggt gtttgttagt actgtgaagg caaaaatgct ttctacattg 1380
acattcattc ctattttact gggcacctat gaatgtatgc tgtgtgctag aaatagacta 1440
aaacatattc ctatagcatg ttagtgttt tgcatgtttg ctgaaaatcc tttgtgtata 1500
aaccagtttg taaggttctc tgggttaggt agggactctg cagtttcttc ctgtcaaaat 1560
ctctcctacc aagatggtgt tccactgtcc agcccagcat gagtagcagg tagagcacag 1620
ctttactggc tgtttgtatg ctttggttta gtgcaatgtg tggtagatta cttatcagaa 1680
aacatatatg tcatctctag aacgaagaaa aagcatagta gttcaattcc cagtgtgtcc 1740
ctttgatttt tttttttaa tagtaaaaat aagaatctgt actgactttt cacttggcca 1800
ttctggtttt aaaggacaag ctacaagctc tgtgtttctg tactgatgtg tcacttatta 1860
aatacttttg taccatgagt aaaacttcag gtgtttcgca agaaccacca ttctcaaaa 1919
<210> 109
<211> 2941
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5595679CB1
attaggetaa taggacagea ettgaatgge ttagggetea accagaetgt tgateteete 60
atgcaagagt caggatgtcg tttagaacat ccttctgcta ccaaattccg aaatcatgtc 120
atggaaggag actgggataa ggcagaaaat gacctgaatg aactaaagcc tttagtgcat 180
tetecteatg ctattgtggt aagaggegea ettgaaatet eteaaaegtt gttgggaata 240
attgtgagga tgaagttttt gctgctgcag cagaagtacc tagaatacct ggaggatggc 300
aaggteetgg aggeacttea agttetaege tgtgaattga egeegetgaa atacaataca 360
gagcgcattc atgttcttag tgggtatctg atgtgtagcc atgcagaaga cctacgtgca 420
aaagcagaat gggaaggcaa agggacagct tcccgatcta aactattgga taaacttcag 480
acctatttac caccatcagt gatgettece ceaeggegtt tacagactet cetgeggeag 540
gcggtggaac tacaaaggga tcggtgccta tatcacaata ccaaacttga taataatcta 600
```

```
gattctgtgt ctctgcttat agaccatgtt tgtagtagga ggcagttccc atgttatacg 660
cagcagatac ttacggagca ttgtaatgaa gtgtggttct gtaaattctc taatgatggc 720
actaaactag caacaggatc aaaagataca acagttatca tatggcaagt tgatccggat 780
acacacctgc taaaactgct taaaacatta gaaggacatg cttatggcgt ticttatatt 840
gcatggagtc cagatgacaa ctatcttgtt gcttgtggcc cagatgactg ctctgagctt 900
tggctttgga atgtacaaac aggagaacta aggacaaaaa tgagccagtc tcatgaagac 960
agtttgacaa gtgtggcttg gaatccagat gggaagcgct ttgtgactgg aggtcagcgt 1020
gggcagttct atcagtgtga cttagatggt aatctccttg actcctggga aggggtaaga 1080
gtgcaatgcc tttggtgctt gagtgatgga aagactgttc tggcatcaga tacacaccag 1140
cgaattcggg gctataactt cgaggacctt acagatagga acatagtaca agaagatcat 1200
cctattatgt cttttactat ttcaaaaaat ggccgattag ctttgttaaa tgtagcaact 1260
cagggagttc atttatggga cttgcaagac agagttttag taagaaagta tcaaggtgtt 1320
acacaagggt tttatacaat tcattcatgt tttggaggcc ataatgaaga cttcatcgct 1380
agtggcagtg aagatcacaa ggtttacatc tggcacaaac gtagtgaact gccaattgcg 1440
gagetgaeag ggeacaeagg tacagtaaac tgtgtgaget ggaacecaea gatteeatee 1500
atgatggcca gcgcctcaga tgatggcact gttagaatat ggggaccagc accttttata 1560
gaccaccaga atattgaaga ggaatgcagt agcatggata gttgatggtg aatttggagc 1620
agacgacttc tgtttaactt aaaattagtc gtattttaat ggcttgggat ttggtgcaaa 1680
caaacatgat tgatagctgg acagacatgc tcgtcatgaa aaaagaacca tttctgaagc 1740
ccgattgggg ccaaacattt acaccttgct tcatagtaac cagttgagat gaagcacgtc 1800
gttagaacgt tgttggacac catgttgaat tattccccca tcggttgtga agaactgtgc 1860
tacattcagg cttacccatt gaactcagta tatatattt tttccttcct gtcttttgtc 1920
tggcaggata ccattcttgt tgctcttctg tgtaatgaag tttaaatgct tgtttggaaa 1980
actttattta acagtttaga aggcttgata gaaagagtgc attagtctga agagtataca 2040
ttggatagga aagaatttcc ttctttgtt tctccaaatc tttccgcctt atttagcttg 2100
agatetttge agettggtte atggatteta geettgeeeg ttgegeagta tatactgate 2160
cagatgataa accagtgaac tatgtcaaaa gcactctcaa tattacattt gacaaaaagt 2220
tttgtacttt tcacatagct tgttgcccg taaaagggtt aacagcacaa ttttttaaaa 2280
ataaattaag aagtatttat aggattaaag tgacttcatt tgtatacatt tggaatctaa 2340
accagettaa aaacagttte etcaatgaet tagatacaca gtataactga tgetettetg 2400
gaataccaca tgagacatgg tcagaaacag tgcttggaag gacattacac aagaaattca 2460
gagtaatgct ttgaagattt ccccctttt gttttattcc tgaaggaaca tcagtacccg 2520
atcttgaaga aattcaagat tcaaaaagaa ttttaaatac accaacatga gacatcagta 2580
gtcagttggt tttcagtaaa gcttgttcca agttgttctc aacttaggra gtaattttgg 2640
tgtgatctag caaaagagta ggaatcagcg atacaaccac tttggaagct tatagtataa 2700
ttgaaattat tagaagaatt cagcaggtta cagacatact taaactggga ttaaaacctc 2760
ataqtcattt ttcttaattg cccttaatat tttgacatat agggatacat aaatttaaag 2820
aatatttttt ctcagttttt tcagatattg ccatactgaa cctcattcta aactggtgct 2880
gtggatagtc tttccctctc ccctcctgtt ttagtttaag gaaaggtttc cttcatggaa 2940
<210> 110
<211> 710
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 5782457CB1
<400> 110
etegeggteg cetggeegtt gteattgtee eteegetgte acetttteaa geeceagget 60
ggctgcttca gaagcccctg accccatgga ggagtgggac gtgccacaga tgaagaaaga 120
ggtggagagc ctcaagtacc agctggcctt ccagcgggag atggcgtcca agaccatccc 180
cgagctgctg aagtggatcg aggacgggat ccccaaggac cccttcctga accccgacct 240
gatgaagaac aacccatggg tggaaaaggg caaatgcacc atcctgtgag ccccgcaccc 300
ggcccctctc acaccatcct gtgagaccac gcccggcccc actcccacca tcttgtaaga 360
ctgtgcccag ccccactcac tccatcctgt gagtcccact cccagcccca ctcccaccat 420
cetgtgagec catgecegge eccaeteaca ceaacetgtg agececaete eeggeeccaé 480
tcacaacatc ttgtaagact gtgcccggcc ccattcactc catcctgtga gaccacgccc 540
ggccccactc actctatcct gtgagaccac gcctggccc actcccacca tcctgtgagc 600
cccactcctg gccccactca caccatccta tgagcccacg cccggcccca ctcccaccat 660
cctgtgaacc ccactccact cgcacgtgat tacagtctgt aaaggtgtga
```

rapiens

_eature

te ID No: 760677CB1

```
tggatagaca gggtccaaaa tgtgaccctt ctaggctggt atcaccatgg 60
 ggctgaggat tctgcagata ggacatcacc acggcagaga tggacagcct 120
 Agaggtgtca gtctaggatg gccaggctgg gtcccccac cccttactca 180
 gttctgtagg gcaagtctca catgaagcta ctcatcattt gcttcgtgtc 240
  cgagagttgg caaagctgat gaaggagcag tagacagcga cccaagcaca 300
  cagggaaaga ccgatttaag gctgcaagga aggagtcctg ggagcatggc 360
  ccaaagccgc ggcctccaga gctgccgcag aaacggttga agacgctgga 420
   ggcagtgc gagccgtacg atttaatgtg gatggcaatt actgcctgac 480
  gacaagacgc tgaagctgtg gaacccgctt cgggggacgc tgctgcggac 540
  eacggotacg aggtgotgga tgoggooggo tootttgaca acagtagtot 600
  /gcggggaca aggcggtggt tctgtggaat gtggcatcag ggcaggtcgt 660
  .ggggccacg cagggaaggt gaacacggtg cagtttagtg aagaggccac 720
    ggeteta ttgattecag tateegetgt tgggattgee geteaeggag 780
    ligacge tggatgagge cagagatgge gtgtecagtg tgaaggtgte 840
  atcctggcag gctccgtgga tggccgcgtg agacgctatg acctaaggat 900
c ttctcagact acgtgggcag ccccatcacc tgcacctgct tcagccggga 960
   ecchantgt ccageetgga etceacattg eggeteetgg acaaagacae 1020
           acaagggcca taagaaccag gaatacaagc tggactgctg 1080
        .... atgtggtcag ctgttctgag gacgggaagg tgttcttctg 1140
      range tggetetgge ectgeetgtg ggtteeggtg tggtgeagte 1200
   accedadag agoodtgoot gotgaccgcc atgggaggca gogtccagtg 1260
   nggcctatg aggcagagga tggagcaggc tgaagccagg ggacccacca 1320
    .ocgagac acagacatgg c
                                                         1351
```

sapiens

feature

te ID No: 1348567CB1

```
geggaegeg tgggetgaag getgtggege geggetgtee ceatteceae 60
     acgctagcat cgctcggctg gcggctccca gctcgccgcg gagcagtccc 120
     ogggaccgga agtggctcgc ggaggctcag aagctagtcc cggagcccgg 180
       .cggagcgc ggtgacggcg ccatgtccct aatctgctcc atctctaacg 240
      paccoatgt gtatecectg tetetaatea tgtttatgag eggeggetea 300
     cattgcggag aatggtaccg accccatcaa caaccagcct ctctccgagg 360
       Jacateaaa gttgctcacc caatccggcc caagcctccc tcagccacca 420
      attotgaaa gotttgcagg atgagtggga tgcagtcatg ccgcacagct 480
  .a ccagcagctg cagacaaccc gccaagagct gtcacacgct ctgtaccagc 540
proge etgeogtgte attgcccgte teaccaagga agteactget gcccgagaag 600
      notgaaacca caggetggee teattgtgee ecaggetgtg ceaagtteee 660
     ngtgggtgcg ggtgagccaa tggatttggg tgagctggtg ggaatgaccc 720
     tcagaagctt caagacaaag ccactgtgct aaccacggag cgcaagaaga 780
     tgtgcctgag gagctggtga agccagaaga gctcagcaaa taccggcagg 840
     egtggggttg cacagtgcca gcattcctgg gatcctggcc ctggacctct 900
   . caccaacaag atcctcactg gtggggcgga taaaaatgtc gttgtgtttg 960
     tgaacaaatc ctggctaccc tcaaaggcca taccaagaag gtcaccagcg 1020
  ca coottoocag gacctggtgt tttctgcttc ccccgatgcc actatcagga 1080
   t ecceaatgee tettgtgtac aggtggtteg ggcccatgag agtgctgtga 1140
```

```
caggeeteag cetteatgee actggegact ateteetgag etecteegat gateagtact 1200
gggctttctc tgacatccag acagggcgtg tgctcaccaa ggtgacagat gagacctccg 1260
gctgctctct cacctgtgca cagttccacc ctgacggact catctttgga acaggaacca 1320
tggactctca gatcaagatc tgggacttga aggaacgtac taatgtggcc aacttccctg 1380
gccactcggg ccccatcact agcatcgcct tctctgagaa tggttactac ctggctacag 1440
cggctgatga ctcctctgtc aagctctggg atctgcgcaa gcttaagaac tttaagactt 1500
tgcagctgga taacaacttt gaggtaaagt cactgatctt tgaccagagt ggtacctacc 1560
tggctcttgg gggcacggat gtccagatct acatctgcaa acaatggacg gagattcttc 1620
actttacaga gcatagegge etgaceaeag gggtggeett egggeateae gceaagttea 1680
tegetteaae aggeatggae agaageetea agttetaeag eetgtaggee etggeeette 1740
tgatggaagc tgggcctcat ctcagtagag gggtagaatt agg
<210> 113
<211> 3453
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1751354CB1
<400> 113
ggcttgcgca ctacgtcccc agccagaggc tcctacccgg tcggggactt ccggaacgcc 60
ggggtgtggt tccgggtcgt gtgcggctcg gggtaatagg gctgctgctc ggccggccgg 120
cggcggcgag cagcaggggc atgagggcta acccgggaag cggcagctga gcgggccggg 180
aggagegeeg gteecegtgg atecegagag tgeagagete ggggeagggg cegggaggeq 240
tgggggagcc gggccctccc ctcaggaacg tgtcccgggg ccgacccggc ccgtagtgtg 300
gaagcagctt caggtaggtg agctcgtgaa acaatatgaa gaggagaaaa tagcctttta 360
aggaaattgg cccacagaaa ggatggcctt cttggacaat ccaactatca ttctagctca 420
tattcgacag tcacatgtga ccagtgatga cacgggaatg tgtgagatgg ttctcattga 480
tcatgatgtt gacctagaga agattcatcc tccttcaatg cctggagaca gtgggtcaga 540
aattcaggga agcaatggtg agactcaggg ctatgtatat gcccagtcag tcgatattac 600
ctcaagttgg gactttggta ttagaagacg ctcaaacaca gctcaaagat tagaacgact 660
ccgaaaagag agacaaaacc agatcaaatg caaaaatatt cagtggaaag aaagaaattc 720
taagcaatca gcccaggagt taaagtcact gtttgaaaaa aaatctctca aagagaagcc 780
tccaatttct gggaagcagt cgatattatc tgtacgccta gaacagtgcc ctctgcagct 840
gaataaccct tttaacgagt attccaaatt tgatggcaag ggtcatgtag gtacaacagc 900
aaccaagaag atcgatgtct acctccctct gcactcgagc caggacagac tgctgccaat 960
gaccgtggtg acaatggcca gcgccagggt gcaggacctg atcgggctca tctgctggca 1020
gtatacaagc gaaggacggg agccgaagct caatgacaat gtcagtgcct actgcctgca 1080
tattgctgag gatgatgggg aggtggacac cgatttcccc ccgctggatt ccaatgagcc 1140
cattcataag tttggcttca gtactttggc cctggttgaa aagtactcat ctcctggtct 1200
gacatccaaa gagtcactct ttgttcgaat aaatgctgct catggattct cccttattca 1260
ggtggacaac acaaaggtta ccatgaagga aatcttactg aaggcagtga agcgaagaaa 1320
aggateceag aaagttteag geeeteagta eegeetggag aageagageg ageeeaatgt 1380
cgccgttgac ctggacagca ctttggagag ccagagcgca tgggagttct gcctggtccg 1440
cgagaacagt tcaagggcag acggggtttt tgaggaggat tcgcaaattg acatagccac 1500
agtacaggat atgcttagca gccaccatta caagtcattc aaagtcagca tgatccacag 1560
actgcgattc acaaccgacg tacagctagg tatctctgga gacaaagtag agatagaccc 1620
tgttacgaat cagaaagcca gcactaagtt ttggattaag cagaaaccca tctcaatcga 1680
ttccgacctg ctctgtgcct gtgaccttgc tgaagagaaa agccccagtc acgcaatatt 1740
taaactcacg tatctaagca atcacgacta taaacacctc tactttgaat cggacgctgc 1800
taccgtcaat gaaattgtgc tcaaggttaa ctacatcctg gaatcgcgag ctagcactgc 1860
cegggetgae tactttgete aaaaacaaag aaaactgaac agacgtacga getteagett 1920
ccagaaggag aagaaatccg ggcagcagtg acactggcct ccagcctcaa tctgttccgt 1980
agetcagage etgectgeca gggccaagtg cectagagee caeeeggtgt cetgaagtee 2040
tcggggggag gccagcccct ggctcactgg cacagggcag gtgggctctc ggggaaggtg 2100
tegggggeee cetaggaggg agegetgggg acattgeeat gggaeggaag tetgettgge 2160
agtggctttg ataagcgatg cttgggggtc agaccacccc ctagaggagc cacgtgccgc 2220
ccagccacct tcaatgcctg ccaccctgcc cgaggatgta cagagccgtg cccacacatt 2280
tccttgcaac ttgatcaaat ttcttaaagc aaacaacaaa aatgtacatt tctgtttttc 2340
cttttaataa acaggtgtac tctttatcat ggttggtatg atggaccatt ctttggggcg 2400
gaggattgat tatgttactc tctttaaaat ctgttcccat attgaacagg cagattggaa 2460
```

```
aagctatggt tcgatttctc agaagaaatg tttaggtctt agtcaatagt tttaactatg 2520
ccatttgttt aaatgagtgc atttgcttcg agggtagtgt cttactaaaa gttaggaaca 2580
gagacctagt ggtgtgtcca aggccgtgtc actttcccct tcagcacacc ccagcttctg 2640
acctcagagc ccaggagctg cgtggacagt gtggggtgcc aggaggaggg gcggtggctg 2700
gtcctcaggc acgctgcact cccagccaga catggtcttt ccgtttctta agtagcaagt 2760
gtaggtttca gctggcagtt ccacctgcat gttctctgct tcgctgcctt ggaaggggcc 2820
acattececa tteetettet cettacageg cetgeeteet ttttcaagea ggeggaaage 2880
tgctgtttct cacgtttcag ggagagggt gagcggaggg agacctgtgt ccgtgccgtc 2940
cggctccctg ggtgggaaca ggcaagggat cagatgcccc tgacaccacg cctctggcca 3000
caccagatge etetgeagte etegacagee tetteagtgt eceteetgeg gtgatgteet 3060
tactgtcccc agccagggcc ggggaccggt gtttcactga ggacctgcat tagaaacatt 3120
ttttaaattg ttgtacagga agagatgtgt ctaaaacagc atcttaaagc tgagtgtatt 3180
tetttgeaca aggggteatg etgatgaatt ettettteat tetgatettt gtteageeaa 3240
caggagegte etttetaat gtetteeatt eetaeeeece acceaaaac aaaagaaata 3300
tttgtagctt gctatctgta tttgaatttt tagcaatttt atatttagat actttgaaaa 3360
atgtaaatga ctaatttggt cattaaatct tgtgacatat tcgatattaa aatgatatta 3420
aaataaaagt catataaata cacaaaaaaa aaa
<210> 114
<211> 2663
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 1976780CB1
<400> 114
gaaaaaggtt cgaaagaact ggttgtcttc ttgggcggtg ttgcagggtt catctttact 60
ttttaccaaa actcaaggaa gtagcacaag ttggtttggc agtaatcagt ccaaaccaga 120
gttcacagtg gacctcaagg gggcaacaat tgagatggct tcaaaggata aatccagcaa 180
aaagaatgta tttgagctga aaactcgtca aggaacagaa ctgctaattc agtctgacaa 240
tgacactgtt attaatgatt ggtttaaagt tcttagtagt acaatcaata atcaggcagt 300
agaaactgat gaaggaattg aagaggagat accggattca ccaggaatag aaaagcatga 360
taaagaaaag gaacaaaagg atcccaaaaa gcttcgttcc tttaaagtat ctagcataga 420
ttcttcagaa cagaaaaaaa ccaagaaaaa cttaaagaag tttcttacac gacgcccac 480
tttgcaagct gttcgtgaaa aaggttatat taaagatcag gtatttggat ccaatctcgc 540
taatctgtgt cagagagaga atggcacagt accaaagttt gtgaagttat gtattgaaca 600
tgttgaagaa catggtttgg atattgatgg gatatacaga gtaagtggca acctcgcagt 660
gatccagaaa ctaaggtttg cagtcaatca tgatgagaaa ttggacttga atgacagtaa 720
atgggaagat attcatgtca ttactggagc cctcaaaatg ttttttcgag aattaccaga 780
acctetttt acatttaate attttaatga ttttgttaat geaattaage aagaaceaag 840
acagegagte getgetgtta aggacetaat cagacagttg ecaaagecaa accaagacae 900
aatgcagatt cttttccgac atctcagaag agttatagaa aatggagaga aaaatcgaat 960
gacctatcag agtatagcaa ttgtttttgg tcccactcta ttaaaaccag aaaaagagac 1020
tggtaatata gcagttcata ctgtgtacca gaatcagatt gtagaattaa ttcttctgga 1080
actgagttcc atcttcggac gttgattctt actgaagaca acctgtggaa tagaagctgg 1140
attccatcag atttcaaatg tttatacaca atgtatttta ttttttggac caagcagtga 1200
ctctttgatt ttgcactttt tttttgaggg atcagaaggg aaggggagag tcgagatgtg 1260
tgttaggccc tcatatttgc tgctttgttg caagttgata taactgcgtg taattatgaa 1320
ttcattttat cctgaatgtt tgcatttcat actctgaatt tcagtaaaaa tcaaaactta 1380
aaattctaac cagtcatata cactggataa tttggtaaga aaactgtatt ttttttccct 1440
gaaattggat aatgtacttt cttctcaaga ttcatgactt gatagaacaa tactttcagt 1500
tatgttgcaa aggctcttgg gcattttaaa caaaatgaag tatatccatt ttgaaacctg 1560
tgtatttctt tttcggggtt tctgcatgca gtggcagtct taagtgccaa aattcattat 1620
aaccccaaaa taaccccttg atgaaggett getgtetttt actgtgttac acagcatect 1680
tactggatat cttagttgct tgtttgggca gcacactaat attacttaaa acactgtgat 1740
atactggagt tttagttagc ggaagtcagt tcagggcatt ttagggctgt cttgctatac 1800
tgaattgtag ctaacaatcc taattatatc tagtaccata ctgagttatt ggtatgaccc 1860
tgtggaaaca cacattattt tatgtaaata taggctaaag acttaatgtc ctttagcttg 1920
tgtatataat tgtgttgtat agtctcagag tacattctaa ccctacattt ctaatcattg 1980
ttattggtaa tettttetgt gaatattagg ttteeteeag aaatggteeg ttatttggga 2040
aagttaactg tgtgcacttt tagatattaa ctacatttac aggcaaatca ctgtaatgag 2100
```

```
aatggtactg gaaaaatact gaatagactt gctaaatggc acatgcacta caagaggaac 2160
cttttgggtt atttaatatg tacagaaaac attagaaaaa atttattaca gaattctaat 2220
tccagtatga atagtggaaa cccatctgta aattagatgg atgttggatg gaaaatgaca 2280
ttgctaaatt tgagaatttc tttttaccta ctaatgtaga ttgctttgta taataaaaca 2340
cagggtttgg aaggttttgt tacagggagc atggtctgtt gaagattttt aaaatgtatt 2400
tttctagatt aacttctgta catgaaatgt ctaataaaac tataagaggt ttagagattt 2460
ttccattgga aatgtgcatt ttggtttcta atttttttgt tttttcattt actggcatac 2520
tgttatacct catttttaaa aatcaactga atccaatatt tcctgtggca aataacactt 2580
toctcattte atacetttte tectetete catgecaaca tttetecace cacaaegtae 2640
actotttatt tctcatcaat att
                                                                 2663
<210> 115
<211> 1218
<212> DNA
<213> Homo sapiens
<221> misc_feature
<223> Incyte ID No: 2048234CB1
gcctgttgca gccatggtgc attgcagttg cgtgttgttc agaaagtatg gaaatttcat 60
cgataagcta agactettea ceaggggagg ateeggtgga atgggttate etegtttagg 120
acaacttaaa gacaggtatc ctcggaaacg gtttgtggct ggagtaggag caaacagcaa 240
aattagtgca ctgaaaggct ccaaaggaaa agactgggaa atccctgtgc ctgtgggtat 300
ttcagtaact gatgaaaatg gtaaaattat aggagaactc agtaaagaaa atgacagaat 360
tttggtagct caaggaggtc ttggtggtaa attacttaca aatttcttac cattgaaagg 420
ccagaaacga ataattcacc ttgatctaaa acttatagct gatgtaggcc tagtaggatt 480
cccaaatgct ggaaaatcct ctttgctaag ttgtgtttct catgcaaaac ctgcaattgc 540
agattacgca tttacaacat taaagctgaa gctcggaaag ataatgtaca gtgatttcaa 600
acagatatca gtagctgatc ttccgggttt aatagaagga gcacatatga acaaaggaat 660
gggccacaaa ttcctcaagc atatagaaag aactagacaa ctactttttg ttgttgatat 720
tictggattt cagetttett eteacaetea atacaggaca gettttgaaa ecataataet 780
gettacaaaa gagttggaat tgtacaaaga ggaactteay acaaaacetg cactettgge 840
agttaataaa atggacttgc cagatgccca agataagttc catgaattga tgagccagct 900
ccagaatcct aaagattttc tgcatttatt tgaaaaaaac atgattccag agaggactgt 960
agagttccaa catatcatcc ccatatctgc agttactgga gaaggaatcg aagaattaaa 1020
gaattgtata agaaagtcac tggatgaaca ggccaaccag gaaaatgatg cacttcataa 1080^{\circ}
gaaacagttg cttaatttgt ggatttctga tacaatgtct tctactgagc caccatcaaa 1140
qcatqctqtt actacttcca aaatggatat aatttaaata tattaaaaat ggtattgatg 1200
                                                                 1218
qaacagtaaa aaaaaaaa
<210> 116
<211> 1286
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2111754CB1
<400> 116
cccgccttga acttctggac tagcccctcg attgttgtag atgccaagcg gacctcgcgc 60
cgctctgcgt tgggccagcc cctcacagct ggtttcttac cacgtattgc gcaacggaat 120
ctatgcctgt tacccacact ccctgcgccc ccgcaccccg ctcctgtgcg caagtcggaa 180
tataaaaccg cggaggagtg agctcttggg gtgtccagtt ggttgccgcg gcagtctctc 240
cgagcagcgc atttgtcttc taggctgctt ggttcgtgcc tccgagaaag gggtctcctg 300
ctgccagcta agtgtgggag aacttgtgca cgtatctccc ctccgaatcc caacgatggg 360
taacgccagc tttggctcca aggaacagaa gctgctgaag cggttgcggc ttctgcccgc 420
cctgcttatc ctccgcgcct tcaagcccca caggaagatc agagattacc gcgtcgtggt 480
agtcggcacc gctggtgtgg ggaaaagtac gctgctgcac aagtgggcga gcggcaactt 540
ccgtcatgag tacctgccga ccattgaaaa tacctactgc cagttgctgg gctgcagcca 600
```

```
cggtgtgctt tccctgcaca tcaccgacag caagagtggc gacggcaacc gcgctctgca 660
gcgccacgtt atagcccggg gccacgcctt cgtcctggtc tactcagtca ccaagaagga 720
aaccctggaa gagctgaagg ccttctatga gctgatctgc aagatcaaag gtaacaacct 780
gcataagttc cccatcgtgc tggtgggcaa taaaagtgat gacacccacc gggaggtggc 840
cctgaatgat ggtgccacct gtgcgatgga gtggaattgc gccttcatgg agatttcagc 900
caagaccgat gtgaatgtgc aggagctgtt ccacatgctg ctgaattaca agaaaaagcc 960
caccaccagge ctccaggage ccgagaagaa atcccagatg cccaacacca ctgagaagct 1020
gcttgacaag tgcataatca tgtgagccct gggccttaag agccagctct tcctatcctg 1080
tagogtgtag aaaacgtgga ctcatttcac tatgttacat gtacatggtt gattttgtgc 1140
tgttgtttgg actgtaacat ccatgttgtc aatacgtata ccttgtaagt ggataacttt 1200
tctttttccc aggccagaga attcaaattg ttaaaacatt ggcatttgaa gaggagaaca 1260
aaatgtagca tgatgtattt aaagta
<210> 117
<211> 3057
<212> DNA
<213> Homo sapiens
<221> misc feature
<223> Incyte ID No: 2123286CB1
<400> 117
caaggeteeg geetgegagg agteacatta aetttgetet agaagacaae tttacaagga 60
tctaaaagga acaggattaa agatgactga atactgggtt ccagaaattt aaaacaatca 120
gcttagcaaa tcatatattc ttctgtggag ctgagaattg atgtccgctc ttccccgtga 180
tttggaactt tccaatccca gagaaaagtt gacaaaggga ctgcccagga ctgagtccat 240
atggaagaag aacttcctct tttctctgga gacagtggca agccagtaca ggctactctg 300
tcatctttga agatgttaga tgtgggaaag tggccaattt tttccctttg ttctgaagaa 360
gaactacagt taattcgtca ggcttgtgtc tttggcagtg ctggcaatga agttttatac 420
actacagtaa atgatgagat ttttgtgctt ggcacaaact gctgtggctg tttggggtta 480
ggtgacgtcc agagcaccat tgaacctcgg agactggatt ctttaaatgg caaaaaaata 540
gcctgcctca gctatgggag tggtccacat attgtccttg caacaacaga aggagaagtc 600
tttacctggg gtcaraatgc ttatagccag ctgggcaatg ggacaactaa tcatggttta 660
gtgccctgtc atatctctac taatctgtca aacaaacaag tcattgaagt tgcctgtggg 720
tettaccatt etttggtget aacatetgat ggagaggtat ttgeetgggg ttataataac 780
tctgggcagg taggatctgg atcaacagtt aatcagccaa tccctcgaag agtcactggc 840
tqcctacaaa ataaaqtaqt tqtgaccata gcatgtgggc agatgtgctg catggcagta 900
gtagacacgg gggaggtcta tgtctggggt tacaacggaa acgggcagct tggactcggc 960
aacagtggca accagccaac cccttgcaga gtggcagctt tgcaaggcat ccgtgtccag 1020
agggtcgcct gtggctacgc acacacatta gtattaacag atgaaggcca agtgtatgct 1080
tggggcgcca attcttatgg gcagttgggc actggcaata aaagcaacca gtcctatcct 1140
actectgtea etgtggaaaa ggacaggatt ategagattg cageetgtea etceacaca 1200
acgtctgcgg ccaagacgca gggtgggcac gtgtacatgt ggggccagtg ccggggtcag 1260
teegtgatee teeegeacet caeceactte teetgeactg acgaegtgtt tgeetgettt 1320
gccacgcccg ccgtcacgtg gcgcctcctc tccgtggaac ctgatgacca cctcacagtg 1380
gctgagtcac tgaagaggga atttgacaac ccggacactg cagacctgaa gtttctagtt 1440
gatggaaagt acatttatgc acataaagtc cttctcaaga ttcgatgtga gcattttcgt 1500
togtcattgg aagataacga ggatgatatt gtagaaatga gtgaattttc atatcctgtt 1560
taccgggcct tcctggaata cctatacaca gacagcatca gcctttctcc tgaggaggca 1620
gtaggactgc tagacttggc tacattttat agagaaaatc gtttgaaaaa gctctgccaa 1680
caaactatca agcaaggcat ctgcgaggag aatgccatcg ctctgctctc ggctgcggtg 1740
aagtatgatg cacaggattt agaagaattc tgcttcaggt tttgcataaa ccatctgact 1800
gtagtaacac aaacatcagg ttttgcagaa atggaccatg atctcctgaa gaactttatc 1860
agcaaagcaa gcagagttgg agcctttaaa aattgatccc atctgcagga aagtttttga 1920
gcctttccat ttcccctgca aaagccagag atgaatcact tctctttaat taatagtatg 1980
tatgatgagc tatgtttggc tgagtacttg taactgtcag aagaaggatg gtggtgagtg 2040
gtctttgtct gcctaaaccc agagtttatg tagaaagcat tgaatgttct gatcagatgt 2100
gactaaggtc aaggaaaaaa aattgaaata tcttatttac catttcctct ttttgagtca 2160
cttaaattgg acacctttgg taccctggtc tcagtatatg ctattctggc ccaaatgttc 2220
cattattcag ctggctgata ccacatagat agcttgacaa ggagtgctgt ctgtccttac 2280
cacattttca gcactcagca cagtgccttg tgtataatag gcactcaatt tattataaat 2340
cttcagtatg tcctgagaac agctttagtc atggaatact gggagaagga ataactttca 2400
```

```
caaaataaac ttaaaacagc ctgtaattat tgaggttcat attcttctgg tatatcattc 2460
tgagaaattg tggctaattt agaacattgt ttagaattga caaaaggccc tggcaattaa 2520
attgtcaagg cccaagggct aattttaatt ttctttttac ttggagtcat tcattaattt 2580
ctcacatggg attatggagt atgaagtatt atctttgaat gaaattcctg ggctgatctg 2640
ccttacataa tcacataagg tcctttgctt ttctttgtgt taagagggac ttgcctctgt 2700
aaatgaaaat gacaatgtgc ttttcttgta gttgactttc atgtcactca ctataaaata 2760
gqtctcttaa cctggcacca gtataactat aaagcactag ctgagaagga actgatactt 2820
acatttcatg gacagcatta acaagaatga gataaatttg tactttttag atcaaaacaa 2880
attacctaat tgcaaaagag aaactgaaat ggaacatagt ctcagattct tctaatgtgt 2940
atctcacaat gtcatgtaat gtaaaggaaa cccttttgga attagaattc ttgttctgat 3000
gctgaactat ttggtaataa agtgcttatt tgcagataac agaaaaaaaa aaaaaaa
<210> 118
<211> 1803
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2477507CB1
<400> 118
ggtcgcggcc ttcacgggtt cctcggccgt cctgagtccc aaatcccaag ctggagccgt 60
teageteece tecacegett agagatttgg ggggetetgg eccegteett geggaceatt 120
ccgaggggag tccagaggtg aggccgagga acctccctga ctttgcgggg cgcgccgctc 180
ctgcgtctcc tgccagtctc ccttccttct tttcggtcaa caattgaaaa caaaacgagg 240
aacagcagag gagctactgt ataccgagcc ctcagcattg ttcgtaatct ccgcctgcta 300
acageettgt gaagaaggtg etattettet caacaettta cagatgagga caettgaggt 360
toggagacgt ggagcctctt gcacagctgc ttaagtggtg gtagagccga gatttgaacc 420
ctectaacca tteetttetg eegectactg cageteecag cagagatgat tgaactgttg 480
ctcggggtag ggccccagg tgtcagtaat taacactgtg gatacctccc atgaggacat 540
gattcacgac gcccagatgg actactatgg caccegcctg gcaacctgct catcagacag 600
gtccgtcaaa atctttgatg tgcgcaatgg agggcagatc cttatcgccg acctcagggg 660
tcatgagggt cctgtgtggc aagtggcctg ggctcacccc atgtacggca acatcctggc 720
atcgtgctcc tatgaccgga aagtcattat ctggagagag gaaaacggca cctgggagaa 780
gagccacgag catgcgggac acgactcctc agtgaactcg gtgtgctggg ccccccatga 840
ctacggcctg atcctggcct gtgggagctc ggatggggcc atctccctgc tgacttacac 900
cggggaaggc caatgggaag taaagaagat caacaacgct cacaccattg gctgcaatgc 960
cgtcagctgg gcccctgctg ttgtacctgg aagcctcata gaccacccat cggggcagaa 1020
acccaattac atcaagaggt ttgcatcagg tggctgtgac aacctcatca agctgtggaa 1080
ggaggaggag gacggccagt ggaaggagga gcagaagcta gaagcgcaca gtgactgggt 1140
tegagatgtg geetgggeee cetecategg eetgeecace ageaceateg eeagetgete 1200
ccaggatggt cgtgtgttca tttggacctg tgatgatgcc tcaagcaata cgtggtcccc 1260
taaattgttg cacaagttca acgatgtggt gtggcatgtg agctggtcca tcacagccaa 1320
catcctggct gtctctggtg gagacaataa ggtgaccctg tggaaggagt cagttgatgg 1380
gcagtgggtg tgcatcagtg atgtcaacaa gggccagggc tccgtatcag catcagtgac 1440
agagggccag cagaacgagc agtgacaaga caggtggggc ctggctcccc acccgccagc 1500
tocaggactg coccttoctg ggccaactaa ccagacaact gggaagagcc cccaactcca 1560
acaggattat tttcccagga ggagttacag atgcagccac agattgatca tctgccttaa 1620
cgtgatcgga gatgctttgt aatctactgt ccagctgaaa gcactcatgt tacgaggaag 1680
aaactacaag tgatgttcaa atctattttg ggtcattttt atgtaccttt gggttcaggc 1740
attatttggg gggttttgtt tccaaaggaa ctaaataaag tcatattgct tataaaaaaa 1800
aaa
                                                                  1803
<210> 119
<211> 4407
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2759119CB1
```

<220>

<221> unsure <222> 4373, 4379 <223> a, t, c, g, or other qqtcqtcatt qqacaaccgc cqcqqqqccc tqqtctctgc tacctqtaqc tqaqqqtqct 60 gttgatgggc agcgcggcgc gctgggaagg ctcgttctcg cgagagttca gctcccttct 120 atacccgtgg ctgcctcagc acctcgagga tcgacatgga cgctctcgag gactacgttt 180 ggccgcgggc aacctcggag cttatactcc tcccagtgac gggtctggag tgcgtggggg 240 accognitytt ggcgggtgag ggtcccgatg tcctggtgta cagcttggac ttttggtgggc 300 atctgcggat gataaagcga gtgcagaacc tgcttggcca ctatcttatc catggcttcc 360 gggtacggcc agagcctaat ggagaccttg acttggaggc catggtggct gtgtttggaa 420 gcaagggact ccgagttgtg aaaattagct ggggacaggg ccacttctgg gagctttggc 480 gctctggcct gtggaacatg tctgactgga tttgggatgc acgctggctt gagggaaata 540 tagecttggc cetgggccac aactcagtgg tgctatatga ceetgtagta gggtgcatec 600 tgcaagaggt gccctgcaca gacaggtgca ccctctcttc agcctgcctg attggagacg 660 cctggaagga gctgaccata gtggcaggtg ctgtttccaa ccagctcttg gtctggtacc 720 cagcaactgc cttagcagac aacaaacctg tagcacctga ccgacgaatc agtgggcatg 780 tgggcatcat cttcagcatg tcatacctgg aaagcaaggg attgctggct acagcttcag 840 aagaccgaag cgttcgtatc tggaaggtgg gcgacctgcg agtgcctggg ggtcgggtgc 900 agaatattgg gcactgcttt gggcacagcg cccgtgtgtg gcaggtcaag cttctagaga 960 attaccttat cagtgcagga gaggattgtg tctgcttggt gtggagccat gaaggtgaga 1020 tcctccaggc ctttcgggga caccagggac gtgggatccg ggccatagct gcccatgaga 1080 ggcaggcctg ggtgatcact gggggtgatg actcaggcat tcggctgtgg cacttggtag 1140 ggcgtgggta ccggggattg ggggtctcgg ctctctgctt caagtcccgt agtaggccag 1200 gtacactcaa ggctgtgact ctggctggct cttggcgact gctggcagtg actgatacag 1260 gggccctgta tctctatgac gtcgaggtca agtgctggga gcagctgcta gaggataaac 1320 atttccagtc ctactgcctg ctggaggcag ctcctggtcc cgagggcttc ggattgtgtg 1380 ctatggccaa tggggaaggt cgtgtcaagg ttgtccccat caacactcca actgctgctg 1440 tggaccagac cctgtttcct gggaaggtgc acagcttgag ctgggccctg cgtggttatg 1500 aggagetect gttgetggea tegggeeetg geggggtagt agettgeeta gagateteag 1560 ccgcaccete tggcaaggee atctttgtca aggaacgttg tcggtacctg ctgcccccaa 1620 gcaagcagag atggcacaca tgcagtgcct tcctaccccc aggtgacttc ctggtgtgt 1680 gtgaccgccg gggctctgtg ctgctattcc cctccagacc aggtctgctc aaggaccctg 1740 gggtgggagg caaggctcgg gctggtgctg gggcacctgt agtgggtagt ggtagtagtg 1800 ggggtgggaa tgctttcact gggttgggcc cagtgtctac cctgccctct ctgcacggga 1860 agcagggtgt gacctcagtc acatgccatg gtggctatgt gtataccata gggcgtgatg 1920 gagectacta ccagetgttt gtacgagacg gccageteca gccagtecta aggeagaagt 1980 cctgtcgagg catgaactgg ctagctgggc tccgtatagt gcccgatggg agcatggtta 2040 tcctgggttt ccatgccaat gagtttgtgg tgtggaaccc tcggtcacac gagaagctgc 2100 acatcgtcaa ctgtggtgga gggcaccgtt cgtgggcatt ctctgatact gaggcggcca 2160 tggcctttgc ttacctcaag gatggggatg tcatgctgta cagggctctg ggtggctgca 2220 cccggccaca cgtgattctc cgggagggtc tgcatggccg tgagatcact tgtgtaaagc 2280 gtgtgggcac cattaccctg gggcctgaat atggagtgcc cagcttcatg cagcctgatg 2340 acctggagec tggcagtgag gggcccgact tgactgacat tgtgatcaca tgtagtgagg 2400 acactactgt etgtgteeta geacteecta caaccacagg etcageecac geacteacag 2460 ctgtttgtaa ccatatctcc tcggtacgtg ctgtggctgt gtggggcatt ggcaccccag 2520 gtggccctca ggatcctcag ccaggcctga ctgcccatgt ggtgtctgcg ggggggggg 2580 ctgagatgca ctgcttcagc atcatggtta ctccggaccc cagcacccca agccgcctcg 2640 cctgccatgt catgcacctt tcgtcccacc ggctagatga gtattgggac cggcaacgca 2700 ateggeateg gatggttaag gtagacceag agaccaggta catgteeett getgtgtgt 2760 aacttgacca gcccggcctt ggcccccttg tggctgcagc ctgtagtgat ggggccgtaa 2820 getetttett ttgeaggatt etgggeggat tetgeagete ettgetgaaa eetteeacca 2880 taagcgatgt gtcctcaagg tccactcctt tacacacgag gcacccaacc agaggcggag 2940 gctcctcctg tgcagcgcag ctactgatgg cagcctggct ttctgggatc tcaccaccat 3000 gctagaccat gactccactg tcctggagcc tccagtggat cctgggcttc cctaccggct 3060 tggcaccccc tecetgacte tecaggecca cagetgtggt atcaacagec tgcacacett 3120 gcccacccgt gagggccacc atctcgtggc cagtggcagt gaagatggat ccctccatgt 3180 cttcgtgctt gctgtggaga tgctacagct agaagaggct gtgggagagg ctgggctggt 3240 accecagetg egtgtgetag aggaatacte tgteecetgt geacatgetg eccatgtgae 3300 aggeeteaag atectaagee caageateat ggteteagee tecattgate aaeggetgae 3360 cttctggcgt ctggggcatg gtgaacccac cttcatgaat agcactgtgt tccatgtgcc 3420

```
tgatgtggct gacatggact gctggcctgt gagccctgag tttggccacc gttgtgccct 3480
tgggggtcag gggcttgagg tttacaactg gtatgactga ggtatcctgc ggtggctggc 3540
gtgctgggca tggggcctgc tcacagacag catggagcag ggaagggctg tctgtgccca 3600
tgctcagcat gccttgaggg gaggaggtgg tggccgtggg ttcctgatgt cggtgcagga 3660
gctgaaggtg agtggagtgc tgccaagaat atgcccgact ccccatgaca agacagaact 3720
ttgtaacaaa cagtaccaat ttattttggc cgtgggtttt tgcttttttt ccagttgatg 3780
actttgtgaa cattcccagg tattggagcc tctgtggcct taaatgtggc tcagtggagg 3840
gagacccagc atagccaggc cagtatggag cacctcacgc acagctctca gaagctgcag 3900
gcggacgaac atctgaccaa agaggtgtgg tcgaggctcc tgaaagagaa agggcctgct 3960
ggtctcatcc tctgcttcct ttgcctttac cctatacctc tctgcacgtc ccaccccgtt 4020
ttgctgtgtg ctcaccccca ggatgtgtac ccggttgtag taggagctga aatccatgct 4080
gagetgtace aggaacttge atatetagag acagagactg agteactgge ceatetett 4140
gctcttgtgc cccaggccag aataaagaat agagtgtaga gtgtcctggt tgtctatgcc 4200
tcaccatctc tgtgcgtaca gcaatgtgga ccccggggct gtgcagtcca gcactgctgt 4260
ccggctcagc agatccggaa agggaggata ctgttgaaga gcaacaacca ctcacctgt 4320
ttggggagaa aagtgcttgg aaggggaatc caggctcctt gtgccagtaa cangagggnc 4380
aatcactcat catgtagcag tgagaag
<210> 120
<211> 959
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2823818CB1
<400> 120
cccacqcqtc cqcccacqcq tccqggagcg tggagcgccg ggactgtgca cgcttgaccg 60
gaagcccaga ccagtgcggt cctagccaga gagaaaggac atttgccaac aatgagacac 120
gaagegeeea tgeagatgge etetgeeeaa gatgeeaggt aeggeeagaa agaeteetet 180
gatcagaact ttgactacat gttcaaatta ctcatcatcg gcaatagcag tgtggggaaa 240
acatetttte tatteegtta tgeagatgae teetttacat etgeattegt eageacagtt 300
gggatcgatt tcaaagtaaa aactgtattc aaaaatgtaa agagaatcaa gcttcagatt 360
tgggacacag caggccagga aagatacagg actatcacca cagcctatta tcgtggagcc 420
atgggcttta ttttaatgta tgacattaca aatgaagaat ccttcaatgc agtacaagat 480
tggtcaactc aaatcaaaac atactcttgg gacaatgccc aagttattct ggttgggaac 540
aagtqtqaca tggaagacga gcgggtcatc tcaactgagc gaggtcaaca tttaggagaa 600
cagcttgggt ttgagttttt tgaaacaagt gccaaggaca acattaatgt caagcagaca 660
tttgagcgcc ttgtggatat catctgcgac aaaatgtcag agagtttgga gactgatcct 720
gccatcactg ctgcaaagca gaacacgaga ctcaaggaaa ctcctcctcc accgcagccc 780
aactgtgcct gctagtgtcc ccgtgcacac aggcagctcc agggggctct ggttgccaac 840
aaacagcatt tgtaaatggt ctattagcct tcatttatac tgcctaacaa ttatttgaag 900
<210> 121
<211> 1809
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2859730CB1
<400> 121
ggcagcggtt ggaggcttcg cccggctttg cagcggggac ttcggcggcg gcgcctcagg 60
cacctcggcc cggacacgat gaggcgagtg gtacgacaga gcaagtttcg gcatgtattt 120
gggcaagcgg tgaaaaatga ccagtgctat gatgacatcc gggtttctcg tgtgacctgg 180
gatagttcct tttgtgctgt caatcccaga tttgttgcca taatcataga ggcaagtggg 240
ggaggagegt teettgteet eeetetgege aagaetggte gaattgacaa atettaceet 300
acagtatgtg gccacacagg accagtgctg gacatagact ggtgcccaca taacgatcag 360
gtcattgcca gcggttcaga ggactgcacg gtcatggtat ggcagatccc agaaaatgga 420
ctcaccettt ecetgaetga acetgtggtg attttggaag gecaeteaaa gagagtegge 480
```

```
atcgtggctt ggcatccaac ggcccgcaat gtgcttctta gtgcaggctg tgataatgcc 540
attatcatct ggaatgtggg aacaggggaa gcccttataa acttggacga tatgcattca 600
gacatgattt acaatgtgag ctggaaccgg aatggcagtc tgatctgcac agcttccaaa 660
gacaagaaag tgagagtcat tgatcccagg aaacaagaga ttgttgctga gaaggagaaa 720
gcacatgaag gagcaagacc catgagagcc atcttcctgg ccgatggcaa tgtcttcacc 780
actgggttca gccgcatgag cgagcggcag ctggctctct ggaatccgaa aaatatgcag 840
gaaccaattg ctcttcatga gatggacact agcaatgggg tgttgctgcc tttctatgac 900
cctgacacca gcatcattta cttatgtgga aagggtgaca gcagtattcg ctattttgag 960
atcacggatg aatccccgta cgtccactac ctcaacacat tcagcagcaa ggagcctcag 1020
agagggatgg gttacatgcc caagagggga cttgatgtta acaaatgtga gattgccaga 1080
ttcttcaaac ttcatgagag aaagtgtgaa cctattatta tgactgttcc caggaagtct 1140
gaccttttcc aagatgacct gtatcctgac acagcggggc cagaggccgc gctggaggca 1200
gaaqagtggt tcgaaggcaa gaatgcagac ccaatcctca tctccttgaa gcacgggtac 1260
attccaggca aaaacaggga tctcaaggtg gtcaagaaga acattctgga tagcaagccc 1320
actgcaaaca agaagtgcga cctgatcagc atccccaaga aaaccacaga cacggccagt 1380
gtgcaaaatg aagccaagtt ggatgagatt ttaaaaagaga tcaaatctat aaaagacaca 1440
atotgcaatc aagatgagcg tatttccaag ttagaacagc agatggcaaa gatagcagcc 1500
tgaaggtccc accccaccc ctacagaaaa aatgggagca agaacttgtg cttgggagct 1560
ggttattggt gtggtcctag ggagggcgga aagggaggca ctgccatttg gagacattcc 1620
atttcagatt tgtcaaccag cgataggcca cattccagta agaactcaat ttgtctccca 1680
aatttgcaga aacaaaacgt gatttaaaag ctgagctttt tatcagaaag cttttttgat 1740
qttttaagtg ttatgtgact tgttgaactt tttaaaaaagt gctactttta aaatcccaga 1800
tactctgaa
<210> 122
<211> 2028
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 2861155CB1
<220>
<221> unsure
<222> 1943, 2003
<223> a, t, c, g, or other
<400> 122
tggcgggttc cgtgggtcgc ccgcgaaatc tgatccggga tgcggcgcc caatcggaag 60
gtggaccgaa atcccgcgac agcaagaggc ccgtagcgac ccgcggtgct aaggaacaca 120
gtgctttcaa aagaattggc gtccgctgtt cgcctctcct cccgggagtc ttctgcctac 180
tcccagaaga ggagggaagc acaggtgggt ttctttagct ctgcgtcgga tccctgagaa 240
cttcgaagec atcctggctg aggetaatet cegetgtget teetetgeag tatgaagaet 300
ttqqaqactc aaccgttagc tccggactgc tgtccttcag accaggaccc agctccagcc 360
catcettete eccaegette eccgatgaat aaaaatgegg actetgaact gatgeeaceg 420
cctcccgaaa ggggggatcc gccccggttg tccccagatc ctgtggctgg ctcagctgtg 480
teccaggage taegggaggg ggacccagtt teteteteca eteceetgga aacagagttt 540
ggttccccta gtgagttgag tcctcgaatc gaggagcaag aactttctga aaatacaagc 600
cttcctgcag aagaagcaaa cgggagcctt tctgaagaag aagcgaacgg gccagagttg 660
gggtctggaa aagccatgga agatacctct ggggaacccg ctgcagagga cgagggagac 720
accgcttgga actacagctt ctcccagctg cctcgatttc tcagtggttc ctggtcagag 780
ttcagcaccc aacctgagaa cttcttgaaa ggctgtaagt gggctcctga cggttcctgc 840
atcttgacca atagtgctga taacatcttg cgaatttata acctgccccc agagctgtac 900
catgagggg agcaggtgga atatgcagaa atggtccctg tccttcgaat ggtggaaggt 960
gataccatet atgattactg etggtattet etgatgteet eageceagee agacacetee 1020
tacgtggcca gcagcagccg ggagaacccg attcatatct gggacgcatt cactggagag 1080
ctccgggctt cctttcgcgc ctacaaccac ctggatgagc tgacggcagc ccattcgctc 1140
tgcttctccc cggatggctc ccagctcttc tgtggcttca accggactgt gcgtgttttt 1200
tccacggccc ggcctggccg agactgcgag gtccgagcca catttgcaaa aaagcagggc 1260
cagageggca teateteetg catageette ageecagece ageeceteta tgeetgtggc 1320
tectacggee geteectggg tetgtatgee tgggatgatg geteecetet egeettgetg 1380
ggagggcacc aagggggcat cacccacctc tgctttcatc ccgatggcaa ccgcttcttc 1440
```

```
traggagere geaaggatge tgageteetg tgetgggate teeggeagte tggttaceea 1500
etgtggtece tgggtegaga ggtgaecace aateagegea tetaettega tetggaeceg 1560
accgggcagt tectagtgag tggcagcacg ageggggetg tetetgtgtg ggacaeggae 1620
gggcctggca atgatgggaa gccggagccc gtgttgagtt ttctgcccca gaaggactgc 1680
accaatggcg tgagcctgca ccctagcctg cctctcctgg ccactgcctc cggtcagcgt 1740
gtgtttcctg agcccacaga gagtggggac gaaggagagg agctgggcct tcccttgctc 1800
tocacqcqcc acgtccacct tgaatgtcgg cttcagctct ggtggtgtgg ggggggcca 1860
tcgtgggggg cgtgatataa aanggtgttt gagtggctgt gactccttcc tacacagggc 1980
cctgataagc ctaggaatgc canagcccag ctgtagggtc ccagtccc
<210> 123
<211> 2223
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3002667CB1
gcgcgcacgt ggggccgggg cggagagagg cgagcaccgg gaaggggagc gtggggccgc 60
tggaatgggt gaatttaagg tecategagt aegtttettt aattatgtte cateaggaat 120
ccgctgtgtg gcttacaata accagtcaaa cagattggct gtttcacgaa cagatggcac 180
tgtggaaatt tataacttgt cagcaaacta ctttcaggag aaatttttcc caggtcatga 240
gtctcgggct acagaagctt tgtgctgggc agaaggacag cgactcttta gtgctgggct 300
caatggcgag attatggagt atgatttaca ggcgttaaac atcaagtatg ctatggatgc 360
ctttggagga cctatttgga gcatggctgc cagccccagt ggctctcaac ttttggttgg 420
ttgtgaagat ggatctgtga aactatttca aattacccca gacaaaatcc agtttgaaag 480
aaattttgat cggcagaaaa gtcgcatcct gagtctcagc tggcatccct ctggtaccca 540
cattgcagct ggttccatag actacattag tgtgtttgat gtcaaatcag gcagcgctgt 600
tcataagatg attgtggaca ggcagtatat gggcgtgtct aagcggaagt gcatcgtgtg 660
qqqtqtcqcc ttcttqtccg atqqcactat cataaqtqtq gactctqctq ggaaggtqca 720
gttctgggac tcagccactg ggacgcttgt gaagagccat ctcatcgcta atgctgacgt 780
gcagtccatt gctgtagctg accaagaaga cagtttcgtg gtgggcacag ccgagggaac 840
agtetteeat ttteagetgg teeetgtgae atetaacage agtgagaage agtgggtgeg 900
gacaaaaccg ttccagcatc acactcatga cgtgcgcact gtggcccaca gcccaacagc 960
gctgatatct ggaggcactg acacccactt agtctttcgt cctctcatgg agaaggtgga 1020
agtaaagaat tacgatgccg ctctccgaaa aatcaccttt ccccaccgat gtctcatctc 1080
ctgttctaaa aagaggcagc ttctcctctt ccagtttgct catcacttag aactttggcg 1140
actgggatcc acagttgcaa caggcaagaa tggggatact cttccactct ctaaaaatgc 1200
agatcattta ctgcacctaa agacaaaggg tcctgagaac attatctgta gctgtatctc 1260
cccatgtgga agttggatag cctattctac agtttctcgg ttttttctct atcggctgaa 1320
ttatgaacat gacaacataa gcctcaaaag ggtttccaaa atgccagcat tccttcgctc 1380
tgcccttcag attttgtttt ctgaagattc aacaaagctc tttgtagcat caaatcaagg 1440
agetetgeat attgtteage tgteaggagg aagetteaag cacetgeatg ettteeagee 1500
tcagtcagga acagtggagg ccatgtgtct tttggcagtc agtccagatg ggaattggct 1560
agctgcatca ggtaccagtg ctggagtcca tgtctacaac gtaaaacagc taaagcttca 1620
ctgcacggtg cctgcttaca atttcccagt gactgctatg gctattgccc ccaataccaa 1680
caaccttgtc atcgctcatt cggaccagca ggtatttgag tacagcatcc cagacaaaca 1740
gtatacagat tggagccgga ctgtccagaa gcagggcttt caccaccttt ggctccaaag 1800
ggatactect ateacacaca teagtitica teccaagaga eegatgeaca teetieteea 1860
tgatgcctac atgttctgca tcattgacaa gtcattgccc cttccaaatg acaaaacctt 1920
actctacaat ccatttcctc ccacgaatga atcagatgtc atccggaggc gcacagctca 1980
tgcttttaaa atttctaaga tatataagcc tctactcttc atggatcttt tggatgaaag 2040
aacactcgtg gcagtagaac ggcctctgga tgacatcatt gctcagctcc caccacccat 2100
taaaaagaag aaatttggaa cctaaaacag ggcactgtct gtgtccttcc ttgaactgtc 2160
taccctgttg cttttcacaa atcatggtaa taaaacaagt tattcttgag gaaaaaaaaa 2220
                                                                2223
<210> 124
```

<211> 728

<212> DNA

```
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3043734CB1
<400> 124
geggegttte tggtggeeag geateeeggt cetegegegt ggegeagete ceategeegg 60
accgacccat gtcgcgcccg cattgggtcc cgggaccccg gcgggagtgc cgcgtccgtc 120
ctttccaqtc gccgggagtc tgagtcgcgg gccacgcggg agtggcggtg gagagcccgc 180
eggtegttat gaggaeggat etaaaatgae eagcaaaegg aaacettgee aaaegeaget 240
caggagatec atcagtgage agttgeggga etceaeggee agageetggg atetgetgtg 300
gaagaacgtc cgggagaggc ggctggcaga aattgaggca aaagaagcat gtgactggct 360
ccgtgctgcc gggttcccgc aatacgctca gttatatgag gattcacaat ttcccatcaa 420
cattgtggct gtcaagaatg atcatgattt tcttgaaaag gaccttgtag aacctctttg 480
caggtaaacc atgtgaagta tttttgtttc tttccactgt tcagtctgca acaggcatca 540
ctatactgaa gggcgagctc agctattcgg caagtattca ctgagtgcct accatgtgcc 600
tgacccaggt gcaggttcta aatgtactac tgttaatgag catgatcagt ttgtgttttc 660
atggagetta aateetagea ggggeetttg gacactagat taggaaaatg acagagaaag 720
aagagaga
<210> 125
<211> 2161
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3294893CB1
<400> 125
qaqqqqaaq aqcttctcqq ctctaqqctc tqqaqtcccq ggagcagtqa qqqqccaccc 60
ggggcacagg aaagggccgc taggggaggg ccgggtgcac tcggggtgtc tgggccgcgg 120
gtctgaggga tgaggaggg ccatggccag cgacggggcc aggaagcaat tctggaagcg 180
cacaacagca agctcccggg cagcatccag cacgtgtatg gtgcccagca ccccccttt 240
gatocactgt tacatggcac tttgctcagg tocacggcca agatgccgac cacaccagtg 300
aaggccaaga gggtcagcac cttccaggag tttgagagca ataccagcga tgcctgggac 360
gctggggagg acgacgatga gctcctggcc atggcggcgg agagcctgaa ctccgaggtg 420
gtcatggaga cggccaaccg tgtgctgcgt aaccacagcc agcggcaggg gcggcccacg 480
ctgcaggagg ggccagggct tcagcagaag cccaggcccg aggcagagcc gccctcaccc 540
cccagcggcg acctccggct ggtgaagtcg gtcagtgaga gccacacgtc ctgtcctgca 600
gaaagtgcca gcgatgccgc ccctctgcag aggtcccagt ctctcccaca ctcggccacc 660
gtcacgctgg gtggcacatc tgaccccagc actctcagca gctcagcgct gagcgaaaga 720
gaggeeteee ggetegacaa gtteaageag etgettgeeg geeceaacae ggaeettgag 780
gaattacgga ggttgagctg gtccggaatc cctaagccag tgcgtccaat gacgtggaag 840
ctcctctcag gttaccttcc cgccaatgta gaccggagac cagccactct ccagagaaaa 900
caaaaagaat attttgcatt tattgagcac tattacgatt ctaggaacga cgaagttcac 960
caggacacat acaggcagat ccacatagac atccctcgca tgagccctga agcgttgatc 1020
ctgcagccca aggtgacgga gatttttgaa aggatcttgt tcatatgggc gatccgccac 1080
ccagccagtg gatacgttca gggtataaat gatctcgtca ctcctttctt tgtggtcttc 1140
atttgtgaat acatagaggc agaggaggtg gacacggtgg acgtctccgg cgtgcccgca 1200
gaggtgctgt gcaacatcga ggccgacacc tactggtgca tgagcaagct gctggatggc 1260
attcaggaca actacacctt tgcccaacct gggattcaaa tgaaagtgaa aatgttagaa 1320
qaactcgtga gccggattga tgagcaagtg caccggcacc tggaccaaca cgaagtgaga 1380
tacctgcagt ttgccttccg ctggatgaac aacctgctga tgagggaggt gcccctgcgt 1440
tgtaccatcc gcctgtggga cacctaccag tctgaaccgg acggcttttc tcatttccac 1500
ttgtacgtgt gegetgettt tetegtgaga tggaggaagg aaatactaga agaaaaagat 1560
tttcaagage tgetgetett cetecagaac etgeceacag eccaetggga tgatgaggae 1620
atcagcctgt tgctggccga ggcctaccgc ctcaagtttg cttttgccga cgcccccaat 1680
cactacaaga aatgagccca ggcccacccg cagctggcct cactgtcccg ggtggcgcgc 1740
cccacctgcc tggctggtgg taggcccctg tgagctggtc ccgggctgct aaaaggcctt 1800
gtgaggtggc cccacctcc aggggagctg gtgaagatgg gccacagacc tggtctaggg 1860
ctgacaaaga cagggacagc ctttgttttc tgagatacca aagagagcca ggggagggcc 1920
```

```
ccgggttcgg cggccagagg caggtcaggg gtcccctctc cctctccctg caatgtcctt 1980
gecaaatgae tgeeteetge tgeecetagt eeggggeage etaggaggee caccetettt 2040
ggagtcctgc tgtctgggtg ccagggccgg aacgaggtag tggccatctc atacctactc 2100
<210> 126
<211> 2782
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3349052CB1
<400> 126
attagetgee ggegtgaett tgaeegette eeggtgegtt aceggeaget gaaeecaeec 60
ggcgtcacgg gactttgacg cgtgctctgc gcttgccatg agactcctgg gagccgcagc 120
cgtcgcggct ctggggcgcg gaagggcccc cgcctcccta ggctggcaga ggaagcaggt 180
taattggaag gcctgccgat ggtcttcatc aggggtgatt cctaatgaaa aaatacgaaa 240
tattggaatc tcagctcaca ttgattctgg gaaaactaca ttaacagaac gagtccttta 300
ctacactggc agaattgcaa agatgcatga ggtgaaaggt aaagatggag ttggtgctgt 360
catggattcc atggaactag agagacaaag aggaatcact attcagtcag cagccactta 420
caccatgtgg aaagatgtca atattaacat tatagatact cctgggcatg tggacttcac 480
aatagaagtg gaaagggccc tgagagtgtt ggatggtgca gtccttgttc tctgtgctgt 540
tggaggggta cagtgccaga ccatgactgt caatcgtcag atgaagcgct acaacgttcc 600
gtttctaact tttattaaca aattggaccg aatgggctcc aacccagcca gggccctgca 660
gcaaatgagg tctaaactaa atcataatgc agcgtttatg cagataccca tgggtttgga 720
gggtaatttt aaaggtatta tagatettat tgaggaaega geeatetatt ttgatggaga 780
ctttggtcag attgttcgat atggtgagat tccagctgaa ttaagggcgg cggccactga 840
ccaccggcag gagctaattg aatgtgttgc caattcagat gaacagcttg gtgagatgtt 900
totggaagaa aaaatoocot ogatttotga tttaaagota goaattogaa gagotaotot 960
gaaaagatca tttactcctg tatttttggg aagcgccttg aagaacaaag gagttcagcc 1020
tettetagat getgttttag aataceteee aaateeatet gaagteeaga actatgetat 1080
tctcaataaa gaggatgact caaaagagaa aaccaaaatc ctaatgaact ccagtagaga 1140
caattcccac ccatttgtag gcctggcttt taaactggag gtaggtcgat ttggacaatt 1200
aacttatgtt cgcagttatc agggagagct aaagaagggt gacaccatct ataacacaag 1260
gacaagaaag aaagtacggt tgcaacggct ggctcgcatg catgccgaca tgatggagga 1320
tgttgaggaa gtatatgccg gagacatctg tgcattgttt ggcattgact gtgctagtgg 1380
agacacattc acagacaaag ccaacagcgg cctttctatg gagtcaattc atgttcctga 1440 tcctgtcatt tcaatagcaa tgaagccttc taacaagaac gatctggaaa aattttcaaa 1500
aggtattggc aggtttacaa gagaagatcc cacatttaaa gtatactttg acactgagaa 1560
caaagagaca gttatatctg gaatgggaga attacacctg gaaatctatg ctcagaggct 1620
ggaaagagag tatggctgtc cttgtatcac aggaaagcca aaagttgcct ttcgagagac 1680
cattactgcc cctgtcccgt ttgactttac acataaaaaa caatcaggtg gtgcaggcca 1740
gtatggaaaa gtaataggtg tcctggagcc tctggaccca gaggactaca ctaaattgga 1800
attttcagat gaaacattcg gatcaaatat tccaaagcag tttgtgcctg ctgtagaaaa 1860
ggggttttta gatgcctgcg agaagggccc tctttctggt cacaagctct ctgggctccg 1920
qtttgtcctg caagatggag cacaccacat ggttgattct aatgaaatct ctttcatccg 1980
agcaggagaa ggtgctctta aacaagcctt ggcaaatgca acattatgta ttcttgaacc 2040
tattatggct gtggaagttg tagctccaaa tgaatttcag ggacaagtaa ttgcaggaat 2100
taaccgacgc catggggtaa tcactgggca agatggagtt gaggactatt ttacactgta 2160
tgcagatgtc cctctaaatg atatgtttgg ttattccact gaacttaggt catgcacaga 2220
gggaaaggga gaatacacaa tggagtatag caggtatcag ccatgtttac catccacaca 2280
agaagacgtc attaataagt atttggaagc tacaggtcaa cttcctgtta aaaaaggaaa 2340
agccaagaac taactttgtt tactgtgagt tgactgactc taattgaatc tgcgtggttt 2400
tgatactttg atggattcca gtggaataaa ttcaggctgc tgaaacaaga aattctgagc 2460
ccaggaagcg ggctcttctt tcttcaaaag aagcccttct tgttcatatt caggagcttc 2520
tgttatattc aaaggtaatt ctatgtctat ctcaactcta ttgattggtt ttatagttta 2580
ttgaaaatcc tcaaataaaa tataattatt actgaaatat gtttaatatt taaggggaaa 2640
agagactaat ttcagttata cttttaagct tagaatgtat gttcatttcc aaattttgta 2700
tcataagagt tttcaacata gagaaaagct gaaaaaatgc aaagaataac cacatacttt 2760
ccatctacct tcctttggta ac
```

```
<210> 127
<211> 3019
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3357264CB1
<220>
<221> unsure
<222> 985
<223> a, t, c, g, or other
<400> 127
tggctgggtc cgcgggcggg ggaaggtgtc ctagcggccc gagcctgcgc tccggattct 60
caggcccatc ctgtggtagg ccgtcccagg caggagttgc ctcggaggat ttggcagcca 120
cgacatccca tcctagcccc gcgatgtgcg gggctgtaat ccccttgcac aaaccggccg 180
gacgtaaatt gcagaatcaa agagctgctt tgaatcagca gatcctgaaa gccgtgcgga 240
tgaggaccgg agcggaaaac cttctgaaag tggccacaaa ctcaaaggtg cgggagcaag 300
tgcggctgga gctgagcttc gtcaactcag acctgcagat gctcaaggaa gagctggagg 360
ggctgaacat ctcggtgggc gtctatcaga acacagagga ggcatttacg attcccctga 420
ttcctcttgg cctgaaggaa acgaaagacg tcgactttgc agtcgtcctc aaggatttta 480
tcctggaaca ttacagtgaa gatggctatt tatatgaaga tgaaattgca gatcttatgg 540
atctgagaca agcttgtcgg acgcctagcc gggatgaggc cggggtggaa ctgctgatga 600
catacttcat ccagctgggc tttgtcgaga gtcgattctt cccgcccaca cggcagatgg 660
gactectgtt cacetggtat gactetetea eeggggttee ggteageeag eagaacetge 720
tgctggagaa ggccagtgtc ctgttcaaca ctggggccct ctacacccag attgggaccc 780
ggtgtgatcg gcagacgcag gctgggctgg agagtgccat agatgccttt cagagagccg 840
caggggtttt aaattacctg aaagacacat ttacccatac tccaagttac gacatgagcc 900
ctgccatgct cagcgtgctc gtcaaaatga tgcttgcaca agcccaagaa agcgtgtttg 960
agaaaatcag ccttcctggg atccngaatg aattcttcat gctggtgaag gtggctcagg 1020
aggetgetaa ggtgggagag gtetaceaac agetacaege ageeatgage caggegeegg 1080
tgaaagagaa catcccctac tcctgggcca gcttagcctg cgtgaaggcc caccactacg 1140
eggeeetgge ceactactte aetgeeatee teeteatega eeaceaggtg aageeaggea 1200
cggatctgga ccaccaggag aagtgcctgt cccagctcta cgaccacatg ccagaggggc 1260
tgacaccett ggccacactg aagaatgate agcagegeeg acagetgggg aagteecact 1320
tgcgcagagc catggctcat cacgaggagt cggtgcggga ggcgagcctc tgcaagaagc 1380
tgcggacgat tgaggtgcta cagaaggtgc tgtgtgccgc acaggaacgc tcccggctca 1440
cgtacgccca gcaccaggag gaggatgacc tgctgaacct gatcgacgcc cccagtgttg 1500
ttgctaaaac tgagcaagag gttgacatta tattgcccca gttctccaag ctgacagtca 1560
cggacttctt ccagaagctg ggccccttat ctgtgttttc ggctaacaag cggtggacgc 1620
ctcctcgaag catccgcttc actgcagaag aaggggactt ggggttcacc ttgagaggga 1680
acgeccecgt teaggtteae tteetggate ettactgete tgeeteggtg geaggageee 1740
gggaaggaga ttatattgtc tccattcagc ttgtggattg taagtggctg acgctgagtg 1800
aggttatgaa gctgctgaag agctttggcg aggacgagat cgagatgaaa gtcgtgagcc 1860
tectggaete cacateatee atgeataata agagtgeeae atacteegtg ggaatgeaga 1920
aaacgtactc catgatctgc ttagccattg atgatgacga caaaactgat aaaaccaaga 1980
aaatctccaa gaagctttcc ttcctgagtt ggggcaccaa caagaacaga cagaagtcag 2040
ccagcacctt gtgcctccca tcggtcgggg ctgcacggcc tcaggtcaag aagaagctgc 2100
cctccccttt cagccttctc aactcagaca gttcttggta ctaatgtgag gaaacaaaca 2160
tgttcaggcc ccgaacattt ccggtgctga ctcggcctta aacgtttgtg ccataatgga 2220
aaatatctat ctatctgttc tcaaatcctg tttttctcat agtgtaaact cacatttgat 2280
gtgtttttat gaaggaaagt aaccaagaaa cctctaggaa ttagtgaaaa aagaactttt 2340
ttgaggtgtg ttactatact gctgtaagtt atttattata taaagtattg taaatagaat 2400
agtgttgaag atatgaaata tggctatttt taatggtgac aattatgact tttagtcact 2460
attaaattgg ggttacctat atcagtacaa tttgtagttg tttccaggtt tggctaataa 2520
tcattcctta acctagaatt cagatgatcc tggaattaag gcaggtcaga ggactgtaat 2580
gatagaatta aattagtgtc actaaaaact gtcccaaagt gctgcttcct aataggaatt 2640
cattaaccta aaacaagatg ttactattat atcgatagac tatgaatgct atttctagaa 2700
aaagtctagt gccaaatttg tettattaaa taaaaacaat gtaggagcag ettttettet 2760
agtttgatgt catttaagaa ttactaacac agtggcagtg ttagatgaag atgctgtcta 2820
caaggtagat aatatactgt ttgatactca aaacattttt cattttgttt aaagtagaag 2880
```

```
ttacataatt ctatatttta agtcttgggt aaaaaagtag ttttacattt tataaagtaa 2940
agatgtaaat gattcagctt taaagctcta tttgacttcc ttcttttgtc tgagatagcg 3000
tccagactgc gaaaagcga
<210> 128
<211> 2312
<212> DNA
<213> Homo sapiens
<221> misc_feature
<223> Incyte ID No: 3576329CB1
<400> 128
geeggegege ggtggggeat ggegggtteg eggggtgegg ggegeaegge ggegeegage 60
gtgcggccgg agaagcggcg gtctgagccc gaactggagc ctgagcccga gccggagccc 120
cccctcctct gcacctctcc tctcagccac agcaccggca gcgattctgg cgtctccgac 180
agcgaggaga gtgtgttctc aggcctggaa gattccggca gtgacagcag tgaggatgat 240
gacgaaggcg acgaggaggg agaggacgga gcccttgatg acgagggcca cagtgggatt 300
aaaaagacca ctgaggagca ggtgcaggcc agcactcctt gcccgaggac agagatggcg 360
agegeeegga ttggggatga gtatgeggag gacagetetg atgaggagga cateeggaac 420
acggtgggca acgtgccctt ggagtggtac gatgacttcc cccacgtggg ctacgacctg 480
gatggcagge gcatctacaa gcccctgcgg acccgggatg agctggacca gttcctggac 540
aagatggacg atcctgacta ctggcgcacc gtgcaggacc cgatgacagg gcgggacctg 600
agactgacgg atgagcaggt ggccctggtg cggcggctgc agagtggcca gtttggggat 660
gtgggettca acccctatga gccggctgtc gacttettca gcggggacgt catgatccac 720
ccggtgacca accgcccggc cgacaagcgc agcttcatcc cctccctggt ggagaaggag 780
aaggtetete geatggtgea egecateaag atgggetgga tecageeteg eeggeeeega 840
gaccccaccc ccagcttcta tgacctgtgg gcccaggagg accccaacgc cgtgctcggg 900
cgccacaaga tgcacgtacc tgctcccaag ctggccctgc caggccacgc cgagtcgtac 960
aacccaccc ctgaatacct gctcagcgag gaggagcgct tggcgtggga acagcaggag 1020
ccaggcgaga ggaagctggg ctttttgcca cgcaagttcc cgagcctgcg ggccgtgcct 1080
gcctacggac gcttcatcca ggaacgcttc gagcgctgcc ttgacctgta cctgtgccca 1140
cggcagcgca agatgagggt gaatgtagac cctgaggacc tcatccccaa gctgcctcgg 1200
ccgagggacc tgcagccctt ccccacgtgc caggccctgg tctacagggg ccacagtgac 1260
cttgtccggt gcctcagtgt ctctcctggg ggccagtggc tggtttcagg ctctgacgac 1320
ggctccctgc ggctctggga ggtggccact gcccgctgtg tgaggactgt tcccgtgggg 1380
ggcgtggtga agagtgtggc ctggaacccc agccccqctg tetgcctggt ggctgcagcc 1440
gtggaggact cggtgctgct gctgaaccca gctctggggg accggctggt ggcgggcagc 1500
acagatcage tgttgagege ettegteeeg eetgaggage eeeeettgea geeggeeege 1560
tggctggagg cctcagagga ggagcgccaa gtgggcctgc ggctgcgcat ctgccacggg 1620
aagccagtga cgcaggtgac ctggcacggg cgtggggact acctggccgt ggtgctggcc 1680
acccaaggcc acacccaggt gctgattcac cagctgagcc gtcgccgcag ccagagtccg 1740
ttccgccgca gccacggaca ggtgcagcga gtggccttcc accctgcccg gcccttcctg 1800
ttggtggcgt cccagcgcag cgtccgcctc taccacctgc tgcgccagga gctcaccaag 1860
aagctgatgc ccaactgcaa gtgggtgtcc agcctggcgg tgcaccctgc aggtgacaac 1920
gtcatctgtg ggagctacga tagcaagctg gtgtggtttg acctggatct ttccaccaag 1980
ccatacagga tgctgagaca ccacaagaag gctctgcggg ctgtggcctt ccacccgcgg 2040
tacccactct ttgcgtcagg ctcggacgac ggcagtgtca tcgtctgcca tggcatggtg 2100
tacaatgacc ttctgcagaa ccccttgctg gtgcccgtca aggtgctgaa gggacacqtg 2160
ctgacccgag atctgggagt gctggacgtc atcttccacc ccacccagcc gtgggtcttc 2220
tecteggggg cagaegggae tgteegeete tteacetage tgttetgeet geetgggget 2280
ggggtggtcg tgctgaagtc aacagagcct tc
<210> 129
<211> 921
<212> DNA
                                                      1.5
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 3805550CB1
```

```
<400> 129
aggcggagtc ggggcggtgt gctgaggtgg gcctgagggc ggagtcgagg tcgggctgaa 60
ggcggagtcg gggagggctg aggtgggcct gaaggcagag tcgaggccat ggcagggccg 120
ggcccaggcc cgggggaccc ggacgagcag tacgatttcc tgttcaagct ggtgctggtg 180
ggcgacgcaa gcgtgggcaa gacgtgcgtg gtgcagcgct tcaagaccgg cgccttctcg 240
gagcgccagg gaagcaccat cggcgtcgac ttcaccatga agacgctgga gatccagggc 300
aagegggtea agetgeagat etgggacaeg geeggeeagg ageggtteeg caccateace 360
cagagetact accgcagtge caatggggee atcettgeet acgacateae caagaggage 420
teetteetgt eggtgeetea etggattgag gatgtgagga agtatgeggg etceaacatt 480
gtgcagctgc tgatcgggaa caagtcagac ctcagcgagc ttcgggaggt ctccttggct 540
gaggeacaga geetggetga geactatgae atcetgtgtg ceattgagae gtetgeeaaq 600
gactogagca acgtggagga ggccttcctg agggtggcca cggagctcat catgcgqcac 660
gggggcccct tgttcagcga gaagagcccc gaccacatcc agctgaacag caaggacatc 720
ggagaaggct ggggctgcgg gtgctgacca ggggccgggc cggcagactg ggggttcccc 780
acctectige tetecceage etgecaagee cageceteca gagecageee teetgggtae 840
cggcaactac agcagccggg tgaagctctg gagctctgca tcctgtggcc tggctgcggg 900
atggaggete teettgagga a
<210> 130
<211> 1291
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 4546403CB1
<400> 130
ctcgagcgaa tcggctcgag agatggctcc ttggcggcat gtgcattttc tcctaatgga 60
agettetttg teactggeae tteatgtggt gatttaacag tgtgggatga teaaatgagg 120
tgtctgcata gtgaaaaagc acatgatctt ggaattacct gctgcgattt ttcttcacag 180
ccagtttctg atggagaaca aggtcttcag ttttttcgac tggcatcatg tggtcaggat 240
tgccaagtca aaatttggat tgtttctttt acccatatct taggttttga attaaaatat 300
aaaagtacac tgagtgggca ctgtgctcct gttctgcctt gtgctttttc ccatgatggg 360
cagatgctag tctcagggtc agtggataag tctgtcatag tatatgatac taatactgag 420 aatatacttc acacattgac tcagcacacc aggtatgtca caacttgtgc ttttgcacct 480
aataccettt tacttgetae tggttcaatg gacaaaacag tgaacatetg gcaatttgae 540
ctggaaacac tttgccaagc aaggagcaca gaacatcagc tgaaqcaatt taccgaagat 600
tggtcagagg aggatgtctc aacatggctt tgtgcacaag atttaaaaga tcttgttggt 660
attttcaaga tgaataacat tgatggaaaa gaactgttga atcttacaaa agaaagtctg 720
gctgatgatt tgaaaattga atctctagga ctgcgtagta aagtgctgag gaaaattgaa 780
gageteagga ceaaggttaa atccettet teaggaatte etgatgaatt tatatgteea 840
ataactagag aacttatgaa agatccggtc atcgcatcag atggctattc atatgaaaag 900
gaagcaatgg aaaattggat cagcaaaaag aaacgtacaa gtcccatgac aaatcttgtt 960
cttccttcag cggtacttac accaaatagg actctgaaaa tggccatcaa tagatggctg 1020
gagacacacc aaaagtaaaa ttgttgatat tgtattattt atattttcag tgatctcatt 1080
tgaatgattt ataggtaaat actaatcaga cattattaaa agcaaaacag gaaaaaggta 1140
aacttettaa atttagttae etataaaaat tgteaatttt cattettaa aaacacatgg 1200
acttactata aaagcctttt tgtactagtg aaaagaatct tcagctatat agaaataaag 1260
ttatacttta aattgcaaaa aaaaaaaaaa a
                                                                    1291
<210> 131
<211> 1836
                                                         -1-
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 4767318CB1
<400> 131
ttttagaagg ttagtgttgg ttctttatt cgattaaaca ggaatacaca tatgtctacc 60
aaagaatagg taagggagaa ataagaacac taaaaaaact cggaatcgtt aagtgtgaag 120
```

```
catatttgga gttaaaagaa ccaaatatta ctaagtaagc agacgcgggc acgcgctgca 180
taccgggatt tgtagtccct tccggggcgg ggtacagcgc gcctgcgcag aggggccgtc 240
gctcttccgg gcgcatgcgt gcggcagcgg cgccaggact gactgcgccg tggaggctgc 300
tgcagtgttg tgagttggaa gctggggagc tcggcatggc ggtccccgct gcagccatgg 360
ggccctcggc gttgggccag agcggccccg gctcgatggc cccgtggtgc tcagtgagca 420
geggeeegte gegetaegtg ettgggatge aggagetgtt eeggggeeac ageaagaege 480
gcgagttcct ggcgcacagc gccaaggtgc actcggtggc ctggagttgc gacgggcgtc 540
gcctagcctc ggggtccttc gacaaqacgg ccagcgtctt cttgctggag aaggaccggt 600
tggtcaaaga aaacaattat cggggacatg gggatagtgt ggaccagctt tgttggcatc 660
caagtaatcc tgacctattt gttacggcgt ctggagataa aaccattcgc atctgggatg 720
tgaggactac aaaatgcatt gccactgtga acactaaagg ggagaacatt aatatctgct 780
ggagteetga tgggcagace attgetgtag gcaacaagga tgatgtggtg acctttattg 840
atgccaagac acaccgttcc aaagcagaag agcagttcaa gttcgaggtc aacgaaatct 900
cctggaacaa tgacaataat atgttcttcc tgacaaatgg caatggttgt atcaacatcc 960
tcagctaccc agaactgaag cctgtgcagt ccatcaacgc ccatccttcc aactgcatct 1020
gtatcaagtt tgaccccatg gggaagtact ttgccacagg aagtgcggat gctttggtca 1080
gcctctggga tgtggatgag ttagtgtgtg ttcggtgctt ttccaggctg gattggcctg 1140
taagaaccct cagtttcagc catgatggga aaatgctggc gtcagcatcg gaagatcatt 1200
ttattgacat tgctgaagtg gagacagggg acaaactatg ggaggtacag tgtgagtctc 1260
cgaccttcac agtggcgtgg caccccaaaa ggcctctgct ggcatttgcc tgtgatgaca 1320
aagacggcaa atatgacagc agccgggaag ccggaactgt gaagctgttt gggcttccta 1380
atgattettg agaggaggtt gtagggagag gaggeeeegg cagaggtett cetteatgtg 1440
gttagtttgg tctgttctct cggagttggt gggcacccta aatatttgta agttggtata 1500
aattgtaaac gtctctggtc aggctgcgca tttcgttctt ttgctttgtc tgtgtattag 1560
ctctttccat tctttgcccc cagcatgagt taactcgcgt ggactctgca gtgcgagtag 1620
tgaccccage atacettgte etetggacet cetgtettet etgettetgg gtgcatggta 1680
gactttgtgg catttgatac aacttggaca atacctagtt tggagggagg ggaatggaag 1740
ggcatggaag tttttttaaa taattaaaaa tatatacata taattttgag aattgagcat 1800
ttaataaact gacttttgtt attatggaaa aaaaaa
<210> 132
<211> 2136
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<223> Incyte ID No: 4834527CB1
<400> 132
ggcgcgccgg gagccggcag acatgccaca gacgctgagt gcctccgaca tggtcacccc 60
aggeageete ageceacee ceacegagee cacagatgge gaacaggetg ggeageeet 120
cctggatgga gcgccatcct cagcctccct ggaaacactg atccagcacc tggtgcccac 180
agccgactac taccccgaga aagcctacat cttcaccttc ctgctgagct ctcgcctctt 240
categagece egggagetee tggeeegggt etgecacetg tgeategage ageageaget 300
ggacaagccg gtgctggaca aggcccgggt ccggaagttc ggccccaaac tgctgcagct 360
gttggccgag tggaccgaga ccttcccaag ggacttccag gaagagtcga ctatcgggca 420
ccttaaggac gtcgtgggcc gcatcgccc ctgtgacgag gcataccgga agaggatgca 480
teageteeta caggetetge accagaaget ggeggetetg egecagggge cagaaggtet 540
ggtgggtgcc gacaagccca tctcctacag gaccaagcca ccagcctcca tccacaggga 600
gctccttggt gtctgcagcg acccctacac actggcccag cagctgaccc acgtggaact 660
ggagcggctg cggcacatcg ggcctgagga gtttgtccag gcctttgtga acaaggaccc 720
tetggceage acaaageeet getteagtga caagaceage aacetggagg ettatgtgaa 780
atggttcaac aggctgtgct acctggtggc aactgagatc tgcatgccag ccaagaagaa 840
geagagggee caggtgattg agttetteat egacgtggee egegagtget teaacategg 900
caacttcaac teceteatgg ceateatete eggeatgaac atgageeetg tetecagget 960
gaagaagacc tgggccaaag tgaggacggc caagtttttc atcctegagc accagatgga 1020
cccaacgggg aatttctgca actacaggac agccctgcgc ggggcggccc accgctccct 1080
gacggcccac agcagccgag agaagattgt cattcctttc ttcagcctgc tcatcaaaga 1140
catctacttc ctgaatgagg gctgcgccaa ccgccttccc aatggacacg tcaactttga 1200
gaaattcctg gagctggcca agcaggtggg ggagttcatc acctggaaac aagtggagtg 1260
tecettegag caagacgeca geateaceca etacetgtae acegeececa tetteagtga 1320
ggatggtctt tatttggctt cttatgaaag tgagagccca gagaaccaaa cagaaaaaga 1380
```

aagatggaaa	gctctaagat	cttctatttt	ggggaagaca	tgaaagcgct	gagctgaggg	1440
acgaggaaga	gctggagccc	gcagaagccg	tccacagccc	tgcctcagtg	gcccagtggg	1500
cagaggccag	ggagtgcctc	actattttgc	aaatgccgac	cctgtggcct	gctgcccgcc	1560
ccccgccccc	cacagtggcc	atacgggcac	aggagacctt	ttatgggact	ttggccctgg	1620
			gcacatgcct			
			tcggcaagga			
			ggtgacatgt			
cagtctgtca	ccacgtggct	tgggaacttc	tggagccaca	gcaggcatca	cggtgcgacg	1860
tgagatgcct	gcgccagccc	cgagcccact	ggcagccact	gccattccac	ccatggtccc	1920
			gcagccccag			
			agctgtggaa			
			gtcccgccac			
		tacgcctaaa				2136

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 25 January 2001 (25.01.2001)

PCT

(10) International Publication Number WO 01/05970 A3

(51) International Patent Classification7: C12N 15/12, C07K 14/47, G01N 33/53, C12Q 1/68, A61K 38/17, C07K 16/18, A01K 67/027

(21) International Application Number: PCT/US00/19698

(22) International Filing Date: 19 July 2000 (19.07.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/144,595 19 July 1999 (19.07.1999) US 60/150,460 23 August 1999 (23.08.1999) US 60/159,849 15 October 1999 (15.10.1999) US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

US	60/144,595 (CIP)
Filed on	19 July 1999 (19.07.1999)
US	60/150,460 (CIP)
Filed on	23 August 1999 (23.08.1999)
US	60/159,849 (CIP)
Filed on	15 October 1999 (15.10.1999)

(71) Applicant (for all designated States except US): INCYTE GENOMICS, INC. [US/US]; 3160 Porter Drive, Palo Alto, CA 94304 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): YUE, Henry [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). BANDMAN, Olga [US/US]; 366 Anna Avenue, Mountain View, CA 94043 (US). HILLMAN, Jennifer, L. [US/US]; 230 Monroe Drive #12, Montain View, CA 94040 (US). LAL, Preeti [IN/US]; 2382 Lass Drive, Santa Clara, CA 95054 (US). AU-YOUNG, Janice

[US/US]; 233 Golden Eagle Lane, Brisbane, CA 94005 (US). REDDY, Roopa [IN/US]; 1233 W. McKinley Avenue, #3, Sunnyvale, CA 94086 (US). YANG, Junming [CN/US]; 7125 Bark Lane, San Jose, CA 95129 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US). LU, Dyung, Aina, M. [US/US]; 55 Park Belmont Place, San Jose, CA 95136 (US). AZIMZAI, Yalda [US/US]; 2045 Rock Springs Drive, Hayward, CA 94545 (US). PATTERSON, Chandra [US/US]; 490 Sherwood Way #1, Menlo Park, CA 94025 (US).

- (74) Agents: HAMLET-COX, Diana et al.; Incyte Genomics, Inc., 3160 Porter Drive, Palo Alto, CA 94304 (US).
- (81) Designated States (national): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPl patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

- With international search report.
- (88) Date of publication of the international search report: 26 April 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: GTP-BINDING PROTEIN ASSOCIATED FACTORS

(57) Abstract: The invention provides human GTP-binding associated proteins (GBAP) and polynucleotides which identify and encode GBAP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of GBAP.

Interr nal Application No PCT/US 00/19698

a. classification of subject matter IPC 7 C12N15/12 C07K14/47 G01N33/53 C12Q1/68 A61K38/17 C07K16/18 A01K67/027 According to International Patent Classification (IPC) or to both national classification and IPC Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C07K G01N C12Q A61K A01K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) STRAND C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. χ DATABASE EMEST_HUM1 [Online] 11-15 Entry/Acc.no. $A\overline{A}679577$, 4 December 1997 (1997-12-04) HILLIER, L. ET AL.: "zj49c09.s1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 453616 3' similar to TR:G1230663 G1230663 SIMILAR TO E. COLI HYPOTHETICAL 22.1 KD PROTEIN IN POLA 3' REGION." XP002148938 the whole document X Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-ments, such combination being obvious to a person skilled in the art. "O" document referring to an oral disclosure, use, exhibition or document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 0 8. 01. Ut 2 October 2000 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

2

Smalt, R

Inter nal Application No PCT/US 00/19698

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PC1/US 00/19698	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to cla	im No.
x	DATABASE EMBL - EMEST_HUM13 [Online] Entry HS1229641, Acc.no. AA429983, 25 May 1997 (1997-05-25) HILLIER, L. ET AL.: "zw60f01.r1 Soares_total_fetus_Nb2HF8_9w Homo sapiens cDNA clone IMAGE:774457 5 similar to SW:YSXC_BACSU P38424 HYPOTHETICAL 22.0 KD PROTEIN IN LON-HEMA INTERGENIC REGION; mRNA sequence." XP002148939 the whole document	11-1	5
A	DATABASE EMBL - EMEST ROD2 [Online] Entry/Acc.no. AI122094, 8 September 1998 (1998-09-08) MARRA, M. ET AL.: "uc46f10.r1 Soares mouse mammary gland NMLMG Mus musculus cDNA clone IMAGE:1401067 5' similar to SW:Y335 MYCGE P47577 HYPOTHETICAL GTP-BINDING PROTEIN MG335.;, mRNA sequence." XP002148940 the whole document		
P,X	DATABASE EMBL - EMHUM2 [Online] Entry/Acc.no. AF161484, 1 February 2000 (2000-02-01) YE, M. ET AL.: "Homo sapiens HSPC135 mRNA, complete cds." XP002148941 the whole document	1,3, 11-1 20,2	5,
P,X	WO 99 58675 A (CHIRON CORP ;HYSEQ INC (US)) 18 November 1999 (1999-11-18) the whole document	11-19	5
A	CLAPHAM, D.E. ET AL.: "New roles for G-protein beta-gamma-dimers in transmembrane signalling." NATURE, vol. 365, 30 September 1993 (1993-09-30), pages 403-6, XP002148967 cited in the application the whole document		
	,		

ational application No. PCT/US 00/19698

Box I Observations whir certain claims wer if und unsearchable (C ntinuation of item 1 if first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 18, 21 and 24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. X Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this International application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-28 all partially
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-28, all partially

A protein with at least 90% identity to seq.ID.1 or biologically active or immunogenic fragment thereof, polynucleotide encoding it, optionally transcriptionally linked to a promoter, cell transformed therewith, transgenic organism comprising said polynucleotide, method for producing said protein using said cell, antibody against said protein, polynucleotides having at least 70% sequence homology to seq.ID.67 of at least 60 nt, method for detecting said nucleic acid by hybridization with a probe of at least 20 nt or by amplification, pharmaceutical composition of the protein, methods for screening for (ant)agonists of the protein or modulators of the proteins expression or activity and compounds identified thereby.

Inventions 2-61: claims 1-28, all partially

Subject matter as defined above under invention 1, but limited to the respective protein/nucleic acid sequences:

- 2. 2 and 68,
- 3. 3 and 69,
- 4. 4 and 70,
- 5. 5 and 71,
- 6. 6 and 72,
- 7. 7 and 73, 8. 8 and 74,
- 9. 9 and 75,
- 10.10 and 76,
- 11.11 and 77,
- 12.12 and 78,
- 13.13 and 79, 14.14 and 80,
- 15.15 and 81,
- 16.16 and 82,
- 17.17 and 83,
- 18.18 and 84,
- 19.19 and 85,
- 20.20 and 86,
- 21.21 and 87,
- 22.22 and 88,
- 23.24 and 90,
- 24.25 and 91,
- 25.26 and 92,
- 26.27 and 93,
- 27.29 and 95,
- 28.30 and 96,
- 29.31 and 97,
- 30.32 and 98,
- 31.33 and 99,
- 32.34 and 100.

```
FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210
                 33.36 and 102,
34.37 and 103,
35.38 and 104,
                 36.39 and 105,
                 37.40 and 106,
                 38.41 and 107,
                 39.43 and 109,
                 40.44 and 110,
                 41.45 and 111,
42.46 and 112,
43.47 and 113,
                 44.48 and 114,
                 45.49 and 115,
                 46.50 and 116,
                 47.52 and 118, 48.53 and 119,
                 48.53 and 119,
49.54 and 120,
50.55 and 121,
51.56 and 122,
52.57 and 123,
53.58 and 124,
                  54.59 and 125,
                  55.60 and 126,
                  56.61 and 127,
                  57.62 and 128,
                  58.63 and 129,
                  59.64 and 130,
                  60.65 and 131, and
                  61.66 and 132.
                  For the sake of conciseness, the first subject matter is
                  explicitly defined, the other subject matters are defined by
                  analogy thereto.
```

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claim 12 of the underlying application relates to a polynucleotide comprising at least 60 nt of a polynucleotide, which has at least 70% sequence identity to a nucleic acid sequence selected from those listed in claim 5. Since the at least 60 nucleotides need not originate from an area of homology with any of the sequences of claim 5, the polynucleotide claimed in claim 12 is not defined in any way. The search of said claim has been limited to nucleic acids comprising a nucleic acid sequence having at least 70% homology to a nucleic acid sequence selected from claim 5 of at least 60 nt in length.

Present claims 20 and 23 refer to agonists and antagonists, respectively, defined by reference to a desirable characteristic or property, namely the fact that they can be obtained by certain screening methods. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to proteins with at least 90% homology to seq.ID.1 and antibodies thereto.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

..iormation on patent family members

Interr nal Application No
PCT/US 00/19698

AU	4187499 A	29-11-1999
AII		Z3-11-1333
ΑU	2095599 A	19-07-1999
EP	1053319 A	22-11-2000
WO	9933982 A	08-07-1999
WO	9938972 A	05-08-1999
ΑU	6263999 A	17-04-2000
WO	0018916 A	06-04-2000
	WO WO AU	WO 9933982 A WO 9938972 A AU 6263999 A

. 670